بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

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قسم

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MONA MAGHRABY

Histological Study on the Potential Role of Exosomes Released from Mesenchymal Stem Cells on Healing of Cutaneous Wound in Adult Male Albino Rats

Thesis

Submitted for Partial Fulfillment of Master's Degree in Histology and Cell Biology

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Dedication

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List of Abbreviations

Abb.	Full term
ANOVA	One-way analysis of variance
BM	Bone marrow
CXC	Cysteine-X-Cysteine
DAB	Diaminobenzidine tetrahydrochloride
DMEM	Dulbecco's modified Eagle's medium
ECM	Extracellular matrix
EGF	Epidermal growth factor
ESCs	Embryonic stem cells
EVs	Extracellular vesicles
FBS	Fetal bovine serum
FGFs	Fibroblast growth factors
H&E	Haematoxylin and eosin
HB-EGF	Heparin binding epidermal growth factor
HGF	Hepatocyte growth factor
HRP	Horse-radish peroxidase
IGF-1	Insulin growth factor-1
IL-1	Interleukin-1
IL-6	Interleukin-6
ILVs	Intraluminal vesicles
INOS	Inducible nitric oxide synthase
K	Keratin
mRNA	Messenger RNA
MSCs	Mesenchymal stem cells
MVB	Multivesicular bodies
NGF	Nerve growth factor
PAS	Periodic Acid Schiff

PBS .....Phosphate buffer saline
PCNA .....Proliferating cell nuclear antigen
PDGF.....Platelet-derived growth factor
RGS .....Rat Grimace Scale
SPSS.....Statistical Package for the Social Sciences
TEM .....Transmission electron microscopy
TGF-α.....Transforming growth factor–αlpha
TGF-ß.....Transforming growth factor–βeta
TNF-α.....Tumor necrosis factor-alpha
VEGF .....Vascular endothelial growth factor

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Abstract

Introduction: Skin wounds are frequent injuries that cause heavy financial burdens at both the familial and societal levels with physical and mental suffering. Recently, the attention of researchers has been attracted to the use of exosomes derived from mesenchymal stem cells (MSCs) as a novel non-cell therapy for skin wound.

Aim: To study the potential effects of exosomes derived from MSCs on the healing of cutaneous skin wound in adult male albino rats.

Materials and methods: five weaned rats were used for isolation of exosomes. Forty-two adult male albino rats were divided into three groups: group I (control group); group II (spontaneous wound healing): in which full thickness skin wound was left for spontaneous healing, and group III (treated skin wound with exosomes): 24 hours after generation of skin wound, rats received single intravenous injection of 1ml phosphate buffer saline containing purified exosomes. Each group was subdivided into two subgroups; subgroup A and subgroup B, where skin specimens were collected after 14 days and 21 days, respectively. Exosomes were isolated from bone marrow derived-MSCs through ultracentrifugation. Then, they were characterized by transmission electron microscope. At the end of experiment, skin specimens were collected from all rats and were subjected to haematoxylin and eosin (H&E), Masson`s trichrome, periodic acid schiff (PAS), and proliferating cell nuclear antigen (PCNA) immunohistochemical technique. Histo-morphometric study and statistical analysis were also done.

Results: Administration of MSCs-derived exosomes in group III showed decreased pain experienced by rats, improved wound healing, enhanced epidermal reepithelization, the regeneration of skin appendages, and better organization of newly formed collagen.

Conclusion: Intravenous injection of MSCs-derived exosomes could be effective in the healing of full thickness skin wound in adult rats.

Key words:

Exosomes, Mesenchymal stem cells, wound healing, cutaneous wound, Histology, PCNA

INTRODUCTION

Skin injuries are frequent injuries that cause heavy financial burdens at both the familial and societal levels with physical and mental suffering. Despite the presence of numerous investigations that focused on accelerating the wound healing process, definitive treatments are still currently unavailable **(Zhang et al., 2015)**.

Full thickness skin injuries extend beyond both epidermis and dermis. Therefore, they are characterized by complete destruction of epithelial regenerative capacity. Healing of such wounds results in scar formation **(Mohamed et al., 2019)**, which means less favorable quality of healing **(Hu et al., 2016)**.

Annually, over 100 million people develop scars because of trauma or even surgeries. These scars usually lead to discomfort and pain. Scars are also associated with disfigurement, social avoidance, and depression. It may also have devastating consequences for patients, including limitation of movement, permanent disability, and poor aesthetic appearance. Surgery and laser therapy are examples of therapeutic measures for scarring. However, they have their limitations, restraining them from being widely introduced into clinical application **(Wang, Hu et al., 2017; Čoma et al., 2021).**