



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم



MONA MAGHRABY



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التوثيق الإلكتروني والميكرو فيلم



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكرو فيلم



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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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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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2021

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

سَبَّحَانَكَ لَا إِلَهَ إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, thanks to Allah the kindest and the most merciful to whom I relate any success in achieving any work in my life.

*I would like to express my sincere thanks and gratitude to **Prof. Dr. Manal Shaaban Hafez**, Professor of Histology and cell biology, Faculty of Medicine, Ain Shams University, for her kind supervision, valuable advice, and consistent encouragement and support. It was such a great honor to work under her guidance.*

*I am particularly very grateful and appreciative to **Prof. Dr. Ghada Galal Hamam**, Professor of Histology and cell biology, Faculty of Medicine, Ain Shams University, for her great help, sincere efforts, and continuous encouragement and support throughout the journey, which made the completion of this work much easier. It was a pleasure working under her supervision.*

*I would further like to thank **Dr. Gehan Abd ElKhalek Ibrahim**, Lecturer of Histology and Cell Biology, Faculty of Medicine, Ain Shams University for her great help and precious instructions throughout this work.*

Finally, I would like to express my sincere gratitude, love, respect, and appreciation to all my professors and my colleagues for their continuous support till this work was completed.

Asmaa Ali Mohamed Ahmed

Dedication

Words cannot describe my love, thanks, gratefulness, and respect to my parents, my brothers, and my fiancé for their warm kindness and genuine support. Without their care, patience, encouragement, and support, I would have never achieved any success. To all of them, I dedicate my work.

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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–alpha
TGF- β	Transforming growth factor–beta
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**).