IMMUNOHISTOCHEMICAL STUDY OF THE EFFECT OF MESOTHERAPY ON SKIN REJUVENATION

Thesis

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بسم الله الرحمن الرحيم

رَبِّ أَوْزِعْنِي أَنْ أَشْكُرَ نِعْمَتَكَ الَّتِي
أَنْعَمْتَ عَلَيَّ وَعَلَى وَالِدَيَّ وَأَنْ أَعْمَلَ
صَالِحًا تَرْضَاهُ وَأَصْلِحْ لِي فِي ذُرِّيَّتِي
إِنِّي تُبْتُ إِلَيْكَ وَإِنِّي مِنَ الْمُسْلِمِينَ

صدق الله العظيم

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List of Abbreviations

Abb.	Full term
AP-1	*Activator protein-1*
CA-MMP	*Cysteine array matrix metallo-proteinase*
CD 8+	*T suppressor cell*
CIS-UCA	*Cis-urocanic acid*
CMMP	*Chicken matrix metalloproteinase*
CRP	*Cell Rejuvenating Process*
ECM	*Extracellular matrix*
EGF	*Epidermal growth factor*
EMMPRIN	*Extracellular matrix metalloproteinase inducer*
FGF	*Fibroblast growth factor*
IDP	*Intradermic profound*
IED	*Intraepidermic*
IGF-BP	*Insulin like growth factor binding protein*
IHD	*Intrahypodermic*
IL	*Interleukin*
INF	*Interferon*
MMPs	*Matrix metalloproteinase**s***
mRNA	*Messenger ribonucleic acid*
MT-MMPs	*Membrane type-matrix metalloproteinase*

PPP	*Point by point*
Pro	*Propeptide*
PUMP	*Putative uterine metalloproteinases*
PUVA	*Psoralen and ultra-violet A*
SLEP	*Sub epidermal low acrogenic band*
TGF	*Transforming growth factor*
TIMPs	*Tissue inhibitor of metalloproteinases*
TNF	*Tumor necrosis factor*
UV	*Ultraviolet*
UVA	*Ultraviolet A*
UVB	*Ultraviolet B*
UVR	*Ultraviolet radiation*

INTRODUCTION

Skin aging can be attributed to extrinsic aging and intrinsic (chronological) aging and is commonly related to increased wrinkling, sagging, and laxity ***(Fisher et al., 1997)***.

Extrinsic aging is generally referred to as photoaging and is caused by repeated exposure to ultraviolet (UV) light. Whereas naturally aged skin is smooth, pale, and fine wrinkled, photoaged skin is coarsely wrinkled and associated with dyspigmentation and telangiectasia. Intrinsic skin aging is largely dependent on genetic factors and is associated with increased fragility and loss of elasticity ***(Jenkins, 2002)***.

Skin aging is associated to an increase of the number and the deepness of wrinkles, a direct consequence of the degradation of macromolecules of the dermis, such as collagens and elastin. In dermis, the matrix metallo-proteinase (MMP) overproduction, which occurs in chronological and photo-induced ageing, is stimulated by oxygenated free radicals. Besides, in the skin areas exposed to sun, such as facial skin, other deleterious effects of UV rays occur, in particular an incomplete collagen synthesis, a skin pigmentation, and a solar elastosis (which appears as a degradation of the cutaneous elastic lattice) ***(Fisher et al., 1996 and Jenkins, 2002)***.

Alterations in collagen, the major structural component of the skin, have been considered to be a cause of skin aging and are observed in naturally aged and photoaged skin ***(Gilchrest, 1989 and Varani et al., 2000)***. Collagen decrease attributable to natural skin aging may arise from its reduced synthesis and increased degradation, with a concomitant increase of MMP expression. Moreover, in aged sun-protected skin, both the number of fibroblasts and their capacity to synthesize procollagen are reduced compared with young skin ***(Varani et al., 2000)***.

However, the mechanisms of collagen destruction in aged skin have not been fully clarified. Collagen destruction is, in part, related to the induction of matrix metalloproteinase (MMP) secreted by epidermal keratinocytes and dermal fibroblasts ***(Gilchrest, 1989)***.

In skin ageing, a disequilibrium occurs in the balance between the synthesis of the extracellular matrix (ECM) and its degradation by MMPs. With increasing age, collagen levels are reduced and MMP secretions increased in sun-protected skin compared with young skin. This disequilibrium leads to an excessive degradation of the extracellular matrix, a characteristic of skin ageing ***(Bodemer et al., 2003)***. Moreover, in aged sun-protected skin, both the number of fibroblasts and their capacity to

synthesize procollagen are reduced compared with young skin ***(Bhupinder, 2010)***.

MMP levels are increased by various stimuli, such as UV light, oxidative stress, and cytokines.Collagenases-1 (MMP-1) degrade collagens, while gelatinases A and B (MMP-2 and MMP-9) degrade elastin. Other MMPs, such as stromelysin 1 (MMP-3), are involved both in the collagen and elastin degradation ***(Sternlicht and Werb, 2001)***.

It is evident that the activity of the MMPs is one of the keys of the skin ageing and that these enzymes have thus to be the target of therapeutic activities ***(Philips et al., 2011)***.

Mesotherapy is the technique of using microinjections of conventional or homeopathic compounds; for example, vitamins, minerals, or aminoacids, to deliver correction as facial rejuvenation ***(Segall, 2007)***.

AIM OF THE WORK

The aim of this work was to objectively study the effect induced by rejuvenation mesotherapy of aged skin through histological and immunohistochemical assessment of tissue expression of MMP- 1 and MMP-9.