Development of Skin Diseases Treatment based on Exosome Derived from Plants, Humans, Medicinal Algae and Fungi

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Article

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Abstract: Advances in the treatment of exosomes have led to the development of new therapeutic methods that hold promising potential for improving the treatment options for skin diseases. The aim of this study is to produce pharmaceutical and cosmetic compounds based on exosomes for the treatment of skin conditions such as eczema, pigmentation disorders, skin sagging and aging, cellular skin regeneration, increased skin moisture, and prevention of skin shedding, among others. This study examines the effects of exosomes derived from plants, humans, medicinal algae, and fungi to treat skin diseases. Spectrophotometric analysis reveals the presence of nucleic acids and proteins in exosome samples, indicating their cargo composition. TEM micrographs demonstrate that the exosome isolation process preserves the integrity of the membrane and the crucial spherical structure for their functionality. DLS analysis confirms that isolated exosomes have a size similar to typical exosome dimensions. MTT assays indicate concentration-dependent cytotoxic effects of exosomes on skin cells, with a calculated IC_{50} representing a significant decrease in cell viability. Real-time PCR shows higher gene expression levels of collagen I and collagen III, indicating the potential of exosomes to enhance collagen synthesis. Tyrosinase enzyme expression analysis demonstrates the influence of exosome treatments on pathways related to melanin production.

Keywords: skin diseases; exosome; plants; humans; medicinal algae; fungi; treatment

1. Introduction

Melanin plays a crucial role in the skin, hair, and eye coloration of humans. However, excessive melanin production can lead to various skin conditions such as freckles, melasma, and even cancer. Therefore, regulating the process of melanogenesis is crucial for treating hyperpigmentation disorders [1–4]. Chemical compounds like hydroquinone and tretinoin are commonly used as skin-lightening agents, but they can cause adverse side effects.To address these limitations, researchers have turned their attention towards natural sources for discovering anti-melanogenic agents. Medicinal plants offer a promising alternative to chemical compounds, as they are known to be milder, non-toxic, and biodegradable [5–7].

Maintaining a balance between collagen synthesis and breakdown is crucial for skin rejuvenation and regeneration. Type I Collagen (80-85%) and Type III Collagen (10-15%) are the

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primary constituents of collagen in the skin [8–10]. As people age, the amount of type I collagen declines while the amount of type III collagen increases. A variety of anti-aging strategies have been developed to improve the appearance of aging skin, including cosmetics, chemical peels, phototherapy, and micro-needling [11–14]. However, these methods often produce less durable results, leading to increased attention on finding approaches that yield more long-term anti-aging effects.

Exosomes are small vesicles found in bodily fluids such as saliva, blood, urine, and serum [15–17]. They play a critical role in intercellular communication under both physiological and pathological conditions [18–20]. Exosomes are capable of passing through membranes and protecting the degradation of proteins and RNAs contained within them, making them effective carriers for transferring various compounds to cells [21–23]. Due to their receptor specificity, lack of immune stimulation, and potential for use as drug carriers, exosomes have been identified as agents for transferring genetic material and treating diseases [24–26]. The contents of exosomes vary depending on their cell origin, with different molecules such as growth factors, proteins, broken nucleic acids, and microRNAs (miRNAs) carried by exosomes from different sources [27–29]. Exosomes can penetrate into axons and regulate the inner mechanisms of nerve repair, leading to improved recovery of damaged areas and peripheral nerves [30–32]. Mesenchymal stem cells (MSCs) contain exosomes that mimic the actions of the MSCs themselves, including tissue damage repair, inhibition of inflammatory responses, and regulation of the immune system [33–35]. Unlike traditional treatments, the use of exosomes carries no risk of aneuploidy or transplant rejection, making them a promising tool for treating diseases such as autoimmunity and cancer as pharmaceutical compounds and nanocarriers for drugs and genes [36–38].

Skin ulcer healing is a serious and currently unsolvable problem, which highlights the urgent clinical need for effective treatment strategies. To address this issue, extensive research has been conducted on the use of exosomes derived from adipose-derived stem cells (ADSCs) [39–42]. The development of pharmaceutical compounds based on ADSC-EXOs has shown great potential for wound healing. ADSC-EXO compounds have been found to modulate immune and inflammatory responses at the site of wounds, while also promoting angiogenesis, skin cell reproduction, collagen regeneration, and preventing wound hyperplasia. Compared to ADSCs, ADSC-EXO drugs have high stability, are not rejected by the immune system, and have simpler dosage control. Additionally, these compounds can serve as combined carriers and scaffolds for treatment, leading to skin repair without scarring [43–46].

Human umbilical cord blood-derived mesenchymal stem cells (UCB-MSCs) have been found to have a significant impact on skin wound healing. Recent studies have shown that exosomes derived from MSCs activate several signaling pathways that are beneficial for wound healing and cell growth [47–50]. Umbilical cord blood-derived Stem Cell Conditioned Media (USC-CM) contains various growth factors that aid in skin rejuvenation [51–53]. Investigations have demonstrated that USC-CM EXOs integrate into human dermal fibroblasts (HDFs) and are involved in cell migration and collagen synthesis. Additionally, USC-CM EXOs are absorbed into human skin and promote the synthesis of type I collagen and elastin, which are critical for skin rejuvenation [54].

As individuals age, the ability of human dermal fibroblasts (HDFs) to produce collagen and regenerate the intercellular matrix gradually declines [55,56]. Human dermal fibroblast-derived exosomes (HDF-XO) have been found to enhance the expression of type I procollagen and significantly reduce MMP-1 expression by decreasing tumor necrosis factor-alpha (TNF-α) and upregulating transforming growth factor beta (TGF-β) [57]. As a result, one potential clinical application of HDF-XO-based medicinal compositions is the correction of facial lines (wrinkles) and reduction of skin aging rate.

Based on the findings obtained, the use of exosomes derived from plants, humans, algae, and edible mushrooms for treating hyperpigmentation and rejuvenation is a promising approach for the cosmetics industry in the future [58,59]. Plant-derived exosomes are environmentally safe due to their small size, low toxicity, and high absorbency, making them a potential next-generation drug delivery system for the treatment of many diseases [60]. Plant-derived exosomes exhibit excellent anti-

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melanogenic and anti-aging (anti-wrinkle) properties, and can be used to reduce melanin and free radicals, resulting in skin lightening and rejuvenation. However, it is important to consider the possible toxic effects of exosomes on the skin. Therefore, additional tests such as allergy skin tests or Ames tests should be conducted before use. Few studies have been conducted on the application of plant-derived exosomes for treating hyperpigmentation, and many of the plants employed are indigenous to Korea and China [61,62].

Nowadays, various herbal compounds are being used in cosmetic formulations. However, plant-based cosmetic products for treating skin blemishes face challenges such as low solubility of plant compounds, low affinity for targets, and weak lightening effects compared to chemical compounds [63]. To address these issues, novel and promising technologies have been developed to enhance the efficacy of cosmetics with natural-plant origins and improve the delivery efficiency of bioactive compounds to the skin [64,65]. Nanotechnologies, for instance, have successfully facilitated the delivery of active ingredients to the skin. Examples of these technologies include Nano Aloe Vera for more effective skin care, Nano Quercetin for delaying cell damage caused by UV rays, Nano Fullerene for collagen regeneration and protection against skin aging, Nano Lutein for maintaining antioxidant activity, and Nano-Resveratrol for protecting skin against ultraviolet rays [66–68]. Additionally, compounds derived from marine plants have been found to regulate skin pigmentation. Given the availability of an extensive range of plants with special medicinal properties in Iran, particularly for treating skin conditions such as eczema, blemishes & melasma, and skin sagging & aging [69–71], extracting exosomes from more accessible plant sources with wide distribution, such as spirulina algae, shiitake mushroom (an edible fungus), and human serum is among the objectives of this study.

Several studies have investigated the effectiveness of exosomes in promoting skin tissue regeneration. Shafei et al. conducted a study where exosomes derived from ASCs were loaded into an alginate-based hydrogel (Alg-EXO) for therapeutic purposes in skin wounds. Using a rat wound model, the Alg-EXO group was compared to a non-treated control group and a group treated with alginate only. The results demonstrated that after 15 days, the Alg-EXO group showed significant improvement in wound closure compared to the other groups. The exosomes exhibited the potential to induce collagen deposition and enhance vascularization, thereby facilitating the wound healing process [72].

In another study, researchers developed an injectable self-healing hydrogel (FHE) using Pluronic F127, oxidative hyaluronic acid (OHA), and poly-ε-L-lysine (EPL), with the ability to release exosomes derived from ASCs. In a diabetic mouse wound model, the released exosomes reduced the healing time of the wound. This effect was attributed to enhanced cell proliferation, faster formation of granulation tissue, re-epithelialization, and collagen remodeling at the wound site. As a result, less scar tissue was observed, indicating improved wound healing [73].

Furthermore, Shi et al. created a chitosan/silk scaffold loaded with exosomes derived from gingival MSCs to promote skin regeneration. While the scaffold alone showed positive effects on wound healing in a diabetic rat skin model, the scaffold containing exosomes exhibited significantly greater healing ability. The exosomes enhanced re-epithelialization and deposition/remodeling of the extracellular matrix (ECM) at the site of injury [74].

In addition, Zhao et al. developed a gelatin methacryloyl (GelMA) hydrogel-based wound dressing incorporated with exosomes derived from human umbilical vein endothelial cells (HUVECs) and applied it to a rat model with a wound defect. The results indicated that the exosomes significantly accelerated the wound healing process by promoting re-epithelialization, collagen deposition, and angiogenesis [75].

Jiang et al. investigated the release and function of psoriatic keratinocyte-derived exosomes. In this study, it was observed that these exosomes are endocytosed by neutrophils. Unlike cytokine-treated keratinocyte-derived exosomes, cytokine-treated psoriatic keratinocyte-derived exosomes significantly induced NETosis (a process by which neutrophils produce and release extracellular traps) and the expression of IL-6, IL-8, and TNF-α in neutrophils. Proteomic analysis revealed that cytokine-treated psoriatic keratinocyte-derived exosomes exhibit a specific protein profile with

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enriched proteins involved in immune-related pathways. Finally, it was shown that cytokine-treated psoriatic keratinocyte-derived exosomes contribute to the development of psoriasis-like skin lesions in a mouse model through immune-mediated mechanisms. Overall, the release of exosomes serves as a means of communication between keratinocytes and neutrophils, highlighting the therapeutic potential of psoriatic keratinocyte-derived exosomes with their specific cargo as candidates for the treatment of psoriasis [76].

These studies collectively highlight the remarkable potential of exosomes in augmenting wound healing by influencing various cellular processes such as collagen deposition, angiogenesis, re-epithelialization, and ECM remodeling. The utilization of exosome-based strategies holds promise in revolutionizing the treatment of skin injuries and disorders, paving the way for more effective therapeutic interventions in the field of dermatology.

2. Materials and Methods

2.1. Choosing Medicinal Plants, Spirulina Algae, and Shiitake Mushrooms

In the beginning, various plants and natural products were chosen and acquired for their potential medicinal properties. These included members of the mint family, umbrella family, Rosaceae family, borage family, beech family (Fagaceae), dwarf pomegranate (Punica granatum L. var. nana), Laurus nobilis, mulberry, Amaryllidaceae family, pistachio, frankincense, plants from the Cucurbitaceae family (such as pumpkin and cucumber), ginger (Zingiber officinale), asparagus, chicory, legumes, Rutaceae family, Asphodelaceae family, as well as spirulina algae and shiitake mushrooms (Figure 1).

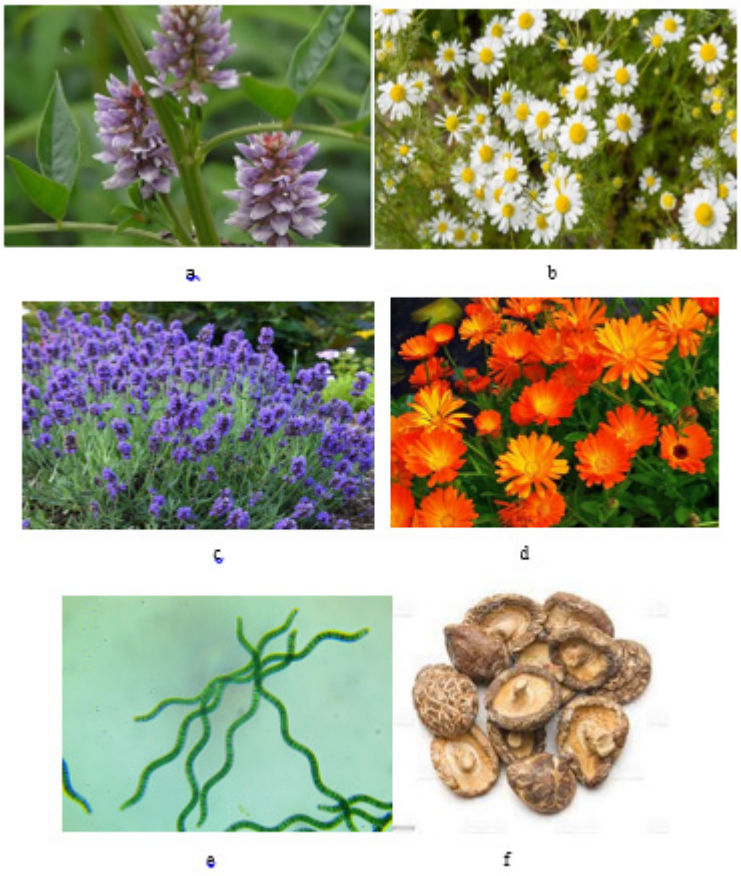

Figure 1. Some examples of plant species are, a) Matricaria chamomilla;b) Glycyrrhiza glabra;c) Lavender;d) Calendula officinalis;e) Spirulina;f) Shiitake Mushroom.

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2.2. Extraction and Production of Essential Oils from Studied Plants

To obtain the extracts and essential oils from the studied plants, fresh and dried plants were first collected. Subsequently, water was extracted from fresh plants and extraction from dried plants was performed using BPS. Finally, for the desired treatment, the selected plants were extracted using the hydrodistillation method (HD) with water.

2.3. Exosome Extraction Methods

The process of extracting exosomes from both human and plant cells follows an identical protocol. Initially, 2 ml of the extracted samples from examined plants and blood serum were separately transferred to micro-tubes. Subsequently, they were centrifuged at 4 degrees Celsius for 10 minutes at a speed of 3000 rpm.

The Exocib S exosome extraction kit, purchased from ANACELL (Supernatants), contains two solutions A and B. Solution A is heated to 37 degrees Celsius during the centrifugation process, following the instructions provided until a completely transparent solution is obtained without any crystals remaining. To achieve this, water is poured into a large petri dish, a thermometer is placed inside, and the solution container is held in the water for a few minutes while being vortexed intermittently. As per the manufacturer's protocol, a 5:1 ratio of sample extract to solution A was taken from the serum samples in both groups using a microliter sampler and transferred to a new microtube. After each dilution, the microtubes were vortexed for a few minutes, and then incubated in a refrigerator at 4 degrees Celsius for 12 hours. The specimens obtained from the previous step were homogenized by vortexing for 1 minute. Subsequently, centrifugation was performed again for 40 minutes at 4 degrees Celsius with a speed of 3000 rpm, and the upper solution was discarded. Finally, 50 microliters of solution B were added to the remaining solution as per the kit manufacturer's standard protocol, and the microtubes were stored at -20°C.

2.4. Formulation for Creating Medicinal and Cosmetic Products

The formulation, content, and composition of constituent components vary depending on the type of product. For example, creams, lotions, and serums are typically prepared using a two-phase system consisting of water and oil, which are held together by an emulsifier. In addition, skin product formulations may also include antioxidants, preservatives, pH regulators, fragrances, additives, and active substances.

2.5. Designing Animal Experiments

In order to evaluate the effects of medicinal products based on human and plant exosomes, twenty Wistar rats were used for animal testing. Exosomes were extracted and the resulting medicinal products were administered to two groups of ten rats each - a treatment group and a control group.

2.6. Measuring Exosome Uptake by Cells Using Spectrophotometric Method

The spectrophotometry method was utilized to confirm the presence of exosomes in cosmetic products and compared to medicinal and cosmetic products without exosomes. Considering that exosomes contain nucleic acids, DNA, RNA, and proteins in various combinations, their absorption was measured using a spectrophotometer at wavelengths ranging from 260 to 280 nm.

2.7. Quality and Structural Verification of Exosomes using Transmission Electron Microscopy (TEM)

Transmission electron microscopy (TEM) was utilized to observe the morphology and structure of exosomes. To prepare specimens for TEM analysis, an exosome suspension was fixed with 1% glutaraldehyde and placed on a carbon-coated grid before being air-dried at room temperature. The grids were subsequently washed with sterile phosphate-buffered saline (PBS) and stained with 2% uranyl acetate (UA) dye for 10 minutes. LEO field-emission scanning electron microscope model

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912AB manufactured in Germany was used to perform morphological studies of the exosomes at 120 KW voltage, and images were captured for examination.

2.8. Measuring Exosome Size and Percentage Using Dynamic Light Scattering (DLS)

This technique is based on the measurement of Brownian motion, which is related to the hydrodynamic diameter and follows Stokes-Einstein equation. Dynamic Light Scattering (DLS) provides results in three forms: intensity, volume, and number. In this study, a phosphate buffer was used as the solvent to determine the diameter size of exosomes using DLS technique, with a refractive index of 1.33 and viscosity of 1.64. The Particle Size Analyzer used for this purpose was Vasco3 model, manufactured by Cordouan Company in France. This device analyzes the size of particles by measuring light radiation and scattering.

2.9. Evaluation of Toxic Properties and In Vitro Survival Rates of Extracted Exosomes

To investigate the toxicity of exosomes on skin cells, the exosomes were thawed and cultured with the desired medium in a CO_2 incubator at 37°C. The cells were then passaged after three days. An MTT assay was used to assess the cytotoxic effect of the exosomes on skin cells at different time points (24, 48, and 72 hours) after incubation.

2.10. Conducting in Vivo Clinical and Molecular Trials

2.10.1. RNA Level Gene Expression Analysis and Real-time Tissue Testing

To examine the gene expression of Collagen I, Collagen III, Homo sapiens prolyl 4-hydroxylase subunit alpha 1, and Elastin, real-time PCR was performed using the Pars Toos kit and analyzed with an ABI device based on the primers designed. Analysis was performed using the primers designed in Table 1, and the results are shown in Figure 5.

Table 1. Designed primers.

Primer	Sequence and Size
Collagen I	forward 5′- ATCAGCCCAAACCCCAAGGAGA -3′
	reverse 5′- CGCAGGAAGGTCAGCTGGATAG -3′, 233bp
Collagen III	forward 5'- TGATGGGATCCAATGAGGGAGA -3'
	reverse 5'- GAGTCTCATGGCCTTGCGTGTTT -3',
Elastin	forward 5′- CTTCCTGGTGGAGTTCCCGGTGGA -3
	reverse 3′- CCGATGCCACCAATACCACCGACA -5′,
PH1	Forward 5′- CGGGATCCTCGGACACCCTGTAAATG
	Reverse 5′ GGAATTCCAAGCAGTCCTCAGCTGT 3′,
GAPDH	Forward 5′-CCATTCTTCCACCTTTGATGCT-3
	Reverse 5′ TGTTGCTGTAGCCATATTCATTGT 3

2.10.2. Exploring Tyrosinase Enzyme Expression

Regulating melanin production in the skin, including exploring tyrosinase enzyme expression, is a crucial strategy for treating hyperpigmentation disorders that interfere with tyrosinase activity. Therefore, given the significance of the tyrosinase enzyme in medicine and pharmaceuticals, and considering that increasing its expression reduces the formation of skin pigments, freckles, and other skin spots, investigation into tyrosinase expression was carried out using SDS-PAGE and western blotting with Bio-Metra electro-blotter.

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2.11. Conducting Clinical Trials on Human Subjects

To evaluate the effectiveness of exosome-based medicinal compounds on humans, a group of 50 healthy individuals and 50 individuals with skin eczema (presenting various symptoms such as pimples, hives, burns, spots, and cracks) were selected under the supervision of an allergy specialist. An allergy test was initially performed to assess any potential toxicity of the exosomes on the subjects' skin. Once it was confirmed that the medicinal compounds based on exosomes did not cause any allergic reactions, clinical trials were conducted on the remaining subjects. Macroscopic evaluation was carried out before and after the treatment. It is worth noting that some individuals were allergic to the herbal components used in the compound, so exosomes derived from their own blood serum were specifically utilized for their treatment.

3. Results

3.1. Spectrophotometric

Samples containing DNA and RNA were exposed to ultraviolet light at a wavelength of 260 nm (260 A), with higher absorption indicating a greater concentration of nucleic acids in the sample containing exosomes. Additionally, increased light absorption at 280 nm indicates a higher protein content in the extracted product.

3.2. TEM

The TEM micrographs revealed that the isolation process preserved the integrity of the exosome membrane, indicating that it remained intact. This is a positive findin gas maintaining the membrane structure is crucial for the stability and functionality of the exosomes.

The micrographs also confirmed that the exosomes exhibited a spherical structure. This is significant because the spherical shape is characteristic of exosomes and is essential for protecting their internal components. The preservation of the membrane-bound spherical structure suggests that the internal cargo, such as nucleic acids and proteins, may also be safeguarded during the isolation process, enhancing the potential therapeutic value of these exosomes.

Furthermore, the analysis determined that the diameter of the examined exosomes was 100 nanometers or less. This size range is consistent with the typical dimensions of exosomes, which often fall in the nanometer scale. The small size of exosomes is noteworthy because it allows them to perform vital cellular functions, including cell-to-cell communication and the transfer of bioactive molecules.

Based on the TEM micrographs, it can be concluded that the structure of the exosomes was successfully preserved during the isolation process. The presence of membrane-bound spherical particles with a diameter of less than 100 nanometers indicates that these exosomes have the potential to fulfill important cellular functions (Figure 2).

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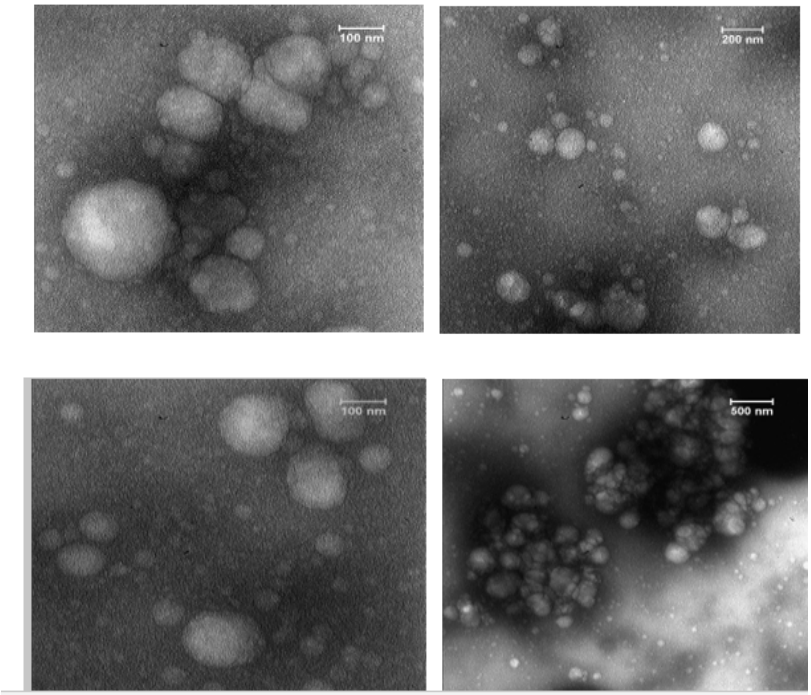

Figure 2. Examination of exosomes using electron microscopy with magnifications of 100, 200, and 500 nm.

3.3. DLS analyses

Based on the results of DLS analyses, it has been determined that more than 80% of the vesicles present in the suspension have a size less than 100 nanometers. This result indicates that the isolated exosomes in this suspension are mainly present in plant, algae, and medicinal fungi species.Exosomes are spherical particles that are protected by a membrane and can have important functions in cells (Figure 3).

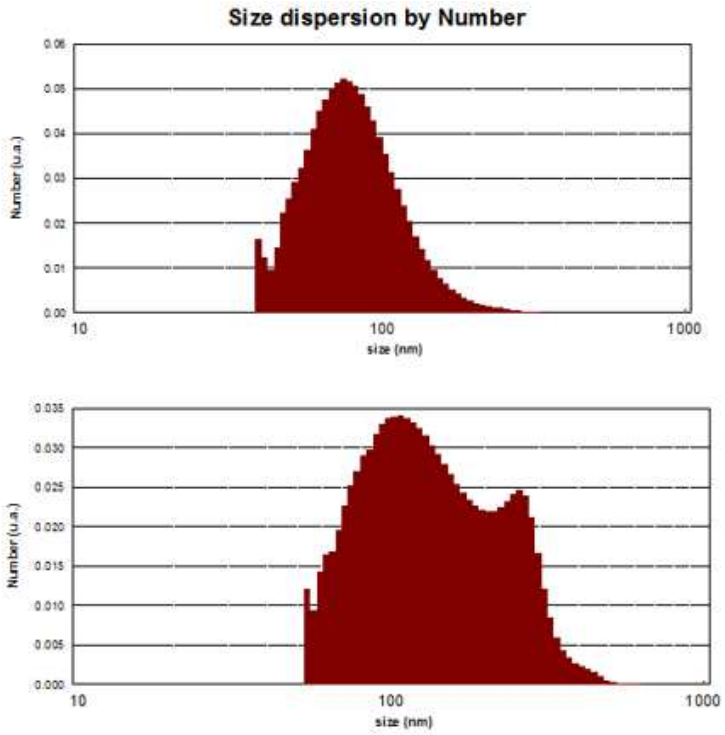

Figure 3. Investigating Exosomes Using Dynamic Light Scattering (DLS).

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3.4. MTT

The study investigated the effects of varying concentrations of exosomes on the survival rate of healthy skin cells, comparing them to a control group (DMEM). The results, as depicted in Figure 4, indicate that as the concentration of exosomes increases, the survival rate of healthy skin cells decreases.

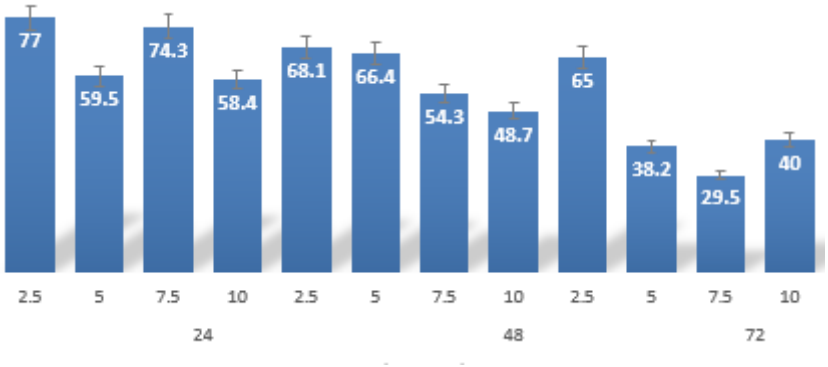

Figure 4. Investigation of the toxicity property and viability of extracted exosomes using the MTT assay on skin epithelial cells of mice treated with drug combinations containing exosomes.

For instance, at a concentration of 5.7 micrograms per milliliter, the survival rate of healthy cells incubated with exosomes reached 5.29 %. This finding suggests that at higher concentrations of exosomes, the viability of healthy skin cells is significantly reduced. It indicates that the exosome treatment has caused cellular toxicity, leading to a decrease in cell survival.

Additionally, the IC_{50} (half-maximal inhibitory concentration) has been calculated at a concentration of 8.2 micrograms per milliliter. The IC_{50} represents the concentration of exosomes at which there is a 50 % reduction in the survival of skin cells. This value serves as an indicator of the concentration threshold at which exosomes exhibit a significant toxic effect on skin cells.

In summary, the results of the study suggest that exosomes derived from plants, humans, medicinal algae, and fungi display cytotoxic effects on skin cells. The degree of cellular toxicity is concentration-dependent, meaning that higher concentrations of exosomes result in a greater reduction in cell viability. The calculated IC_{50} provides valuable information on the concentration at which exosomes cause a 50 % reduction in cell survival.

3.5. Real-time PCR

Figure 5 demonstrates that the gene expression levels of collagen I and collagen III are significantly higher compared to the housekeeping gene GAPDH.

Collagen I and collagen III are well-known proteins associated with the extracellular matrix of the skin. They play crucial roles in maintaining the structural integrity, elasticity, and overall health of the skin. The higher levels of gene expression for collagen I and collagen III in the studied cells indicate that these cells possess an active molecular machinery for the production and synthesis of these important skin-related proteins.

On the other hand, GAPDH is a commonly used housekeeping gene in gene expression studies. It is often employed as a reference gene because its expression is assumed to remain relatively stable across different conditions or treatments. In this context, the expression levels of collagen I and collagen III genes surpassing the expression of GAPDH suggests the preferential and augmented expression of these collagens in the studied cells.

These results provide valuable insights into the cellular processes related to collagen production and suggest that the investigated cells have a high capacity for synthesizing collagen I and collagen III. The upregulation of collagen gene expression implies the potential of exosomes derived from plants, humans, medicinal algae, and fungi to facilitate the treatment and regeneration of skin diseases characterized by impaired collagen synthesis or degradation.

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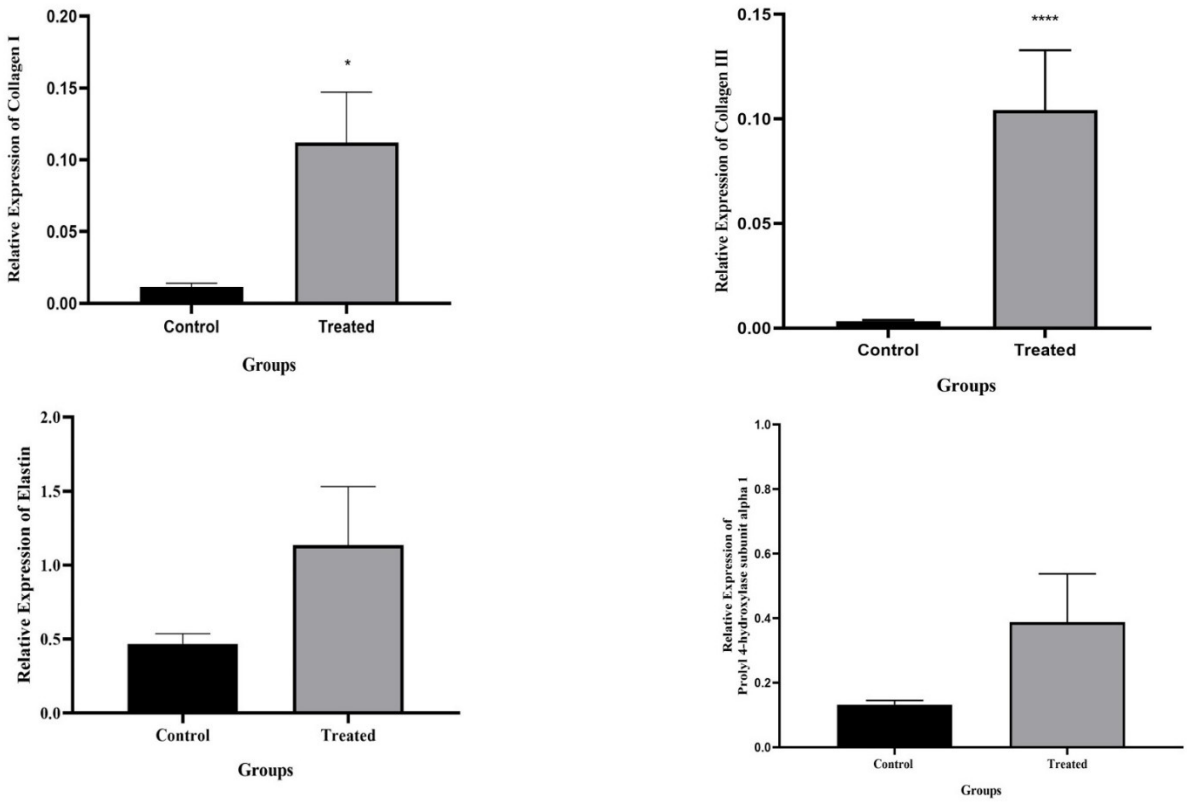

Figure 5. A quantitative analysis of gene expression levels of Collagen I, Collagen III, Homo sapiens prolyl 4-hydroxylase subunit alpha 1, and Elastin using the Realtime PCR assay was performed in control and treated mice.

3.6. Tyrosinase Enzyme Expression

Figure 6 shows the presence of a band with a molecular weight of 58 kilodaltons (kDa), indicating the presence of the tyrosinase enzyme in the epidermal layer of mice treated with Exosome-containing drug combinations.

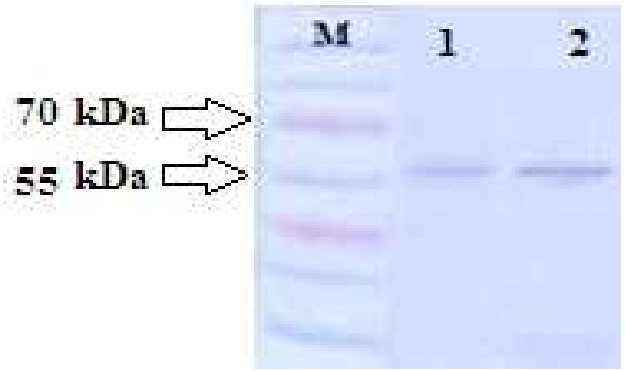

Figure 6. The level of tyrosinase enzyme expression was examined using the Western blotting method to determine the presence of tyrosinase and melanin production in the epidermis of mice treated with a combination of Exosoom drugs.

Tyrosinase is a well-known enzyme involved in melanin production, which plays a crucial role in determining skin and hair color. Melanin is responsible for pigmentation in the skin, hair, and eyes, and its regulation is important in managing skin disorders related to abnormal pigmentation.

The presence of the 58 kDa band, corresponding to the tyrosinase enzyme, suggests that the Exosome-containing drug combinations used in the treatment had an effect on the expression of

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tyrosinase in the epidermis of mice. This finding indicates that the treatment influenced the activity of the enzyme involved in melanin production.

These results provide promising evidence that the Exosome-containing drug combinations used in the study have the potential to modulate tyrosinase expression and, therefore, influence melanin synthesis in the skin. This finding suggests potential therapeutic applications in the treatment of skin diseases characterized by abnormal pigmentation, such as hyperpigmentation or hypopigmentation conditions.

4. Discussion

Authors should discuss the results and how they can be interpreted from the perspective of previous studies and of the working hypotheses. The findings and their implications should be discussed in the broadest context possible. Future research directions may also be highlighted.

In this study, the focus is on the potential of exosomes derived from plants, humans, algae, and mushrooms in the field of dermatology. Exosomes are small vesicles found in bodily fluids and play a crucial role in intercellular communication. They have been studied for their beneficial effects in wound healing, collagen synthesis, skin rejuvenation, and anti-aging.

The study emphasizes the importance of maintaining a balance in melanin production, as excessive melanin can lead to skin conditions and even cancer. Chemical compounds commonly used as skin-lightening agents have limitations, leading researchers to explore natural sources such as medicinal plants. Medicinal plants offer potential advantages in terms of being milder, non-toxic, and biodegradable.

Exosomes derived from adipose-derived stem cells (ADSCs) and umbilical cord blood-derived mesenchymal stem cells (UCB-MSCs) have shown promise in wound healing, promoting collagen synthesis, angiogenesis, and skin cell reproduction. Additionally, human dermal fibroblast-derived exosomes (HDF-XO) have been found to enhance the expression of collagen and reduce the aging rate of skin.

The potential applications of exosomes in treating hyperpigmentation, skin rejuvenation, and aging are also discussed. Plant-derived exosomes, with their anti-melanogenic and anti-aging properties, hold promise as environmentally safe and effective drug delivery systems. However, it is important to consider additional tests for possible toxic effects on the skin. also touches on the use of nanotechnologies to enhance the efficacy of cosmetics with natural-plant origins and improve the delivery of bioactive compounds to the skin.

Medicinal products based on exosomes are currently only available in developed countries, and their production costs for treating various diseases are very high. However, it may be possible to treat many incurable skin diseases inexpensively by using exosomes extracted from plant extracts and medicinal compounds, human blood serum, medicinal mushrooms, and algae. The advancement of biotechnology has led to the evaluation of the interaction between medicinal compounds of plant extracts, blood serum, algae, and medicinal mushrooms. This has resulted in the production of proper medicinal and cosmetic compounds with high performance based on exosomes.

In summary, this study focused on examining the structure of exosomes and their potential effects on skin cells. The results indicated that exosomes are membrane-bound spheres with a diameter of less than 100 nanometers and can have important cellular functions. However, it was also observed that higher concentrations of exosomes can induce cellular toxicity in skin cells. Additionally, gene expression analysis showed high levels of collagen I and collagen III in the studied cells compared to the housekeeping gene GAPDH. Finally, the presence of the tyrosinase enzyme in the epidermis of mice treated with exosome-containing drug combinations suggests that these treatments may have an effect on melanin production. The medicinal products studied in have been found to enhance cell proliferation, synthesis, and penetration of skin collagen, contributing greatly to skin rejuvenation. The effect of exosomes on treating human skin is evident by an increase in the expression of type I collagen and elastin. Studies have shown that the absorption of exosomes in human skin enhances the synthesis of type I collagen and elastin, which are necessary for skin rejuvenation. Therefore, this current study can serve as a benchmark for enhancing wound healing,

promoting collagen formation, reducing water loss in the stratum corneum (SC) area, and treating skin conditions such as eczema, blemishes, melasma, skin sagging, and aging. In addition, it can be effectively utilized as a combination of cosmetic and medicinal products to strengthen and improve the function and quality of the skin. Overall, these findings provide valuable insights into the potential uses and limitations of exosomes in medical research and treatment.

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