

## Review

# Progress of Research on Antioxidants and Carriers for Skin Wound Repair

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**Abstract:** The skin is the first protective barrier of the human body, and oxidative damage is one of the main mechanisms of skin injury. Effective antioxidant therapy plays an important role in skin healing. Therefore, exploring antioxidants and suitable drug delivery methods that can be used for skin injury repair is of great value in regulating skin repair and regeneration and promoting wound healing. Based on this, this paper presents a review of the progress of research on (1) antioxidants and (2) antioxidant carriers for skin repair in order to summarize the research results and provide reference for the subsequent development of new drug-carrier structures and new skin repair strategies.

**Keywords:** skin damage repair; oxidative damage; antioxidants; antioxidant carriers



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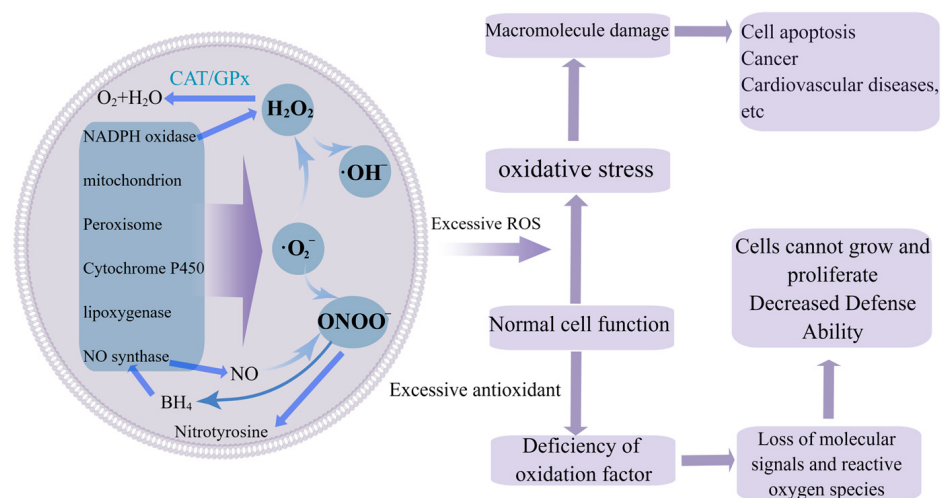
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## 1. Introduction

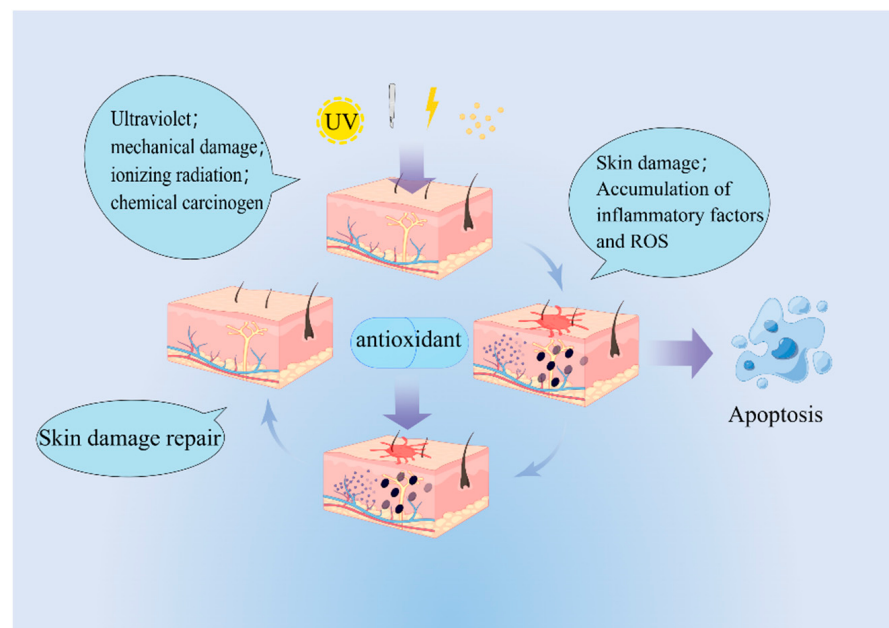
The skin, as the largest organ of the human body, can resist microbial invasion, maintain body fluid and water balance, regulate body temperature and is an important physical protective barrier against external pressure and injury [1]. After a skin injury, the process of wound healing involves inflammation, epithelial remodeling and tissue remodeling [2]. The inflammatory stage of skin tissue regeneration is the key stage of normal wound healing [3]. However, free radicals and reactive oxygen species (ROS) are released from the wound at this stage [4]. The accumulation of these products increases the level of oxidative stress in the cells, destroys the balance between antioxidants and pro-oxidants, affects redox signal transduction, leads to the cell and tissue damage [5] and causes a series of diseases, such as infection [6], delayed wound healing [7], chronic diseases and cancer [8]. Oxidative stress is caused by the excessive accumulation of ROS or metabolites, and when ROS are excessive, a series of free radical chain reactions will lead to oxidative damage in the cells and tissues, seriously affecting cell activity and wound healing [9]. Therefore, the occurrence of a skin injury is closely related to oxidative stress (Figure 1).

Antioxidants are a kind of substances that can help to capture and neutralize free radicals and delay or prevent the oxidation of other chemical substances so as to eliminate the damage of free radicals to the human body, and different antioxidants have different abilities to scavenge free radicals [10]. Antioxidants can not only prevent the related adverse reactions of oxidation but also are one of the important factors in maintaining and

balancing the physiological environment in the body. Using antioxidants to reduce ROS damage is an important research direction in the field of skin damage repair (Figure 2). However, the administration of antioxidants via oral and parenteral routes often requires high doses, repeated doses and long-term treatment, causing adverse effects on human health [2]. Traditional wound dressings are not sufficient to promote hemostasis and adhesion and keep the wound moist [11]. Therefore, in recent years, the development of new drug carriers such as nanofibers and hydrogels has attracted extensive attention. Drug carriers can improve the utilization rate, safety and timeliness of drugs, reduce the frequency of administration, improve the bad odor of drugs and enhance the accuracy of dose administration and release of drugs to targeted tissues and organs [12,13]. Therefore, the selection of suitable antioxidants and their carriers is crucial for the development of novel skin repair materials.



**Figure 1.** The relationship between the amount of intracellular ROS and cell activity. By Figdraw ([www.figdraw.com](http://www.figdraw.com), accessed on 11 June 2023).



**Figure 2.** Schematic diagram of antioxidation and skin damage repair. By Figdraw ([www.figdraw.com](http://www.figdraw.com), accessed on 11 June 2023).

Based on the above, this paper discusses the progress of research on antioxidants and their carriers for skin wound repair, which is mainly divided into two parts: (1) antioxidants and (2) antioxidant carriers. In this paper, the sources of antioxidants are classified, and the carriers that can release drugs are initially discussed in order to provide guidance for the development of novel nanoantioxidants and the study of new skin repair systems.

## 2. Antioxidants

Antioxidants can be roughly divided into two categories: natural antioxidants and artificial antioxidants. Among them, natural antioxidants can be divided into plant antioxidants, animal antioxidants and microbial antioxidants. Artificial antioxidants can be divided into four categories: antioxidants purified by artificial extraction, synthetic antioxidants, nanoantioxidants and gaseous antioxidants. Different types of antioxidants have their own advantages and disadvantages in terms of cost, function and biosafety. Artificial antioxidants are developing in the direction of continuously reducing their side effects and exerting their most appropriate and more effective functions.

### 2.1. Natural Antioxidants

Natural antioxidants come from a wide range of sources mainly divided into three categories: plants, animals and microorganisms. Among them, the plant source is the most extensive, and the peptides from animals have better activity, while the microbial source may bring new inspiration for future treatments.

#### 2.1.1. Plant Antioxidants

In plants, anthocyanins, vitamins, flavonoids, ascorbic acid, polyphenols, etc., are well known as good antioxidants [14–17]. Fruits, vegetables, spices and herbs are generally rich in carotenoids, phenols, polysaccharides, vitamins, trace elements and other antioxidants, which are safe and effective, natural and nontoxic. They inhibit microbial growth and have antioxidative, anti-inflammatory and anti-aging properties [10] (Table 1).

**Table 1.** Some plant metabolites with antioxidant activity [15].

Secondary Metabolites	Common Dietary Sources	References
Ascorbic acid	Peppers, strawberries, kiwifruit and citrus fruits	[16]
Polyphenols	Fruits, vegetables, coffee, tea and cereals	[16,18]
Anthocyanins	Strawberries, black rice, berries, cherries, etc.	[16,19]
Flavones	Blueberries, blood orange juice	[17]
Flavonols	Cherries, chokeberries, elderberries, goji berries (wolfberries)	[17]
Resveratrol	Purple wine, peanuts	[20,21]
Theaflavins	Black tea	[19,22]
Carotenoids	Carrots, tomatoes, pumpkins, peppers, among others	[16,23]
Lycopene	Tomatoes, watermelons, red peppers, papayas, apricots, pink grapefruit	[24,25]

*Perilla frutescens* is rich in antioxidant substances such as polyphenols, which can repair the DNA damage and keratinocytes in the skin exposed to UVB light, and has the effects of antioxidation, anti-inflammation and anti-allergy [26]. Cinnamaldehyde (CIN), the main component of cinnamon, also has strong antioxidant activity [27]. Korean ginseng plays an important role in anti-photodamaging, anti-radiation, anti-inflammatory, antioxidative, anti-aging, anti-melanogenic and wound healing activities [28]. One study [29] found that *Curcuma* species (*Curcuma longa* and *Curcuma aeruginosa*) and curcumin not only influenced the antioxidative and anti-inflammatory process in the production of hyaluronic acid, increased skin moisture and reduced axillary hair growth but also promoted wound healing and prevented chronic UVB injuries. Moreover, *Curcuma* was also found to improve the symptoms of psoriasis and lesions of radiation dermatitis.

*Spirulina* contains antioxidants such as chlorophyll a and carotenoids, which play an important role in its antioxidative system [30]. Microalgae contain a variety of antioxidants

such as carotenoids, ascorbic acid and glutathione, and these antioxidants play an important role in maintaining the normal life activities of microalgae [31].

Fruits and vegetables that we often eat in our daily life also contain a lot of antioxidants. For example, blueberries are rich in bioactive anthocyanins and have significant antioxidative and ROS-scavenging, anti-inflammatory and antibacterial activities [32–34]. Jujube (*Ziziphus jujuba* Mill.) fruit contains a variety of bioactive substances, such as polysaccharides, polyphenols, amino acids, nucleotides, triterpenoid acids, alkaloids and other nutrients, and has antioxidant and other physiological functions [35]. Cabbage contains glucosinolates, which not only has good antioxidant capacity but also plays an important role in cancer prevention [36]. Lotus root contains phenolic compounds, which have strong antioxidant and scavenging capacities against oxidative factors, so it will become a potential material for extracting antioxidants [37].

### 2.1.2. Animal Antioxidants

In nature, antioxidants are also common in animals. They typically include antioxidant peptides, astaxanthin and so on.

Antioxidant peptides are typical antioxidants of animal origin. It has been found that a new peptide named OM-LV20, identified in the skin secretion of odorous frog *Odorrana margaretae*, exhibits antioxidant and strong wound-healing activities in a mouse model of full-thickness skin wounds [38]. Tyrosine-OA1 is also a new type of antioxidant peptide found in amphibians. While having a good antioxidant capacity, it can also promote the healing of injuries and accelerate the recovery of wounded and formation of new epithelial tissues [10]. Astaxanthin is a kind of natural ketocarotenoid, which is widely found in shellfish such as shrimp, crabs and oysters. It has good antioxidant properties and also shows anti-inflammatory, immunoregulatory, DNA-repairing and anti-photodamaging properties [39].

One study [40] showed that subcutaneous injection of hucMSC-ex (exocrine bodies derived from the mesenchymal stem cells of the human umbilical cord) can have an antioxidative and anti-inflammatory effect on ultraviolet-radiation-induced apoptosis and DNA damage and promote skin regeneration and repair. Another study [41] showed that laminin from the cells of the mouse dorsal skin can reduce the concentration of peroxide ions in the cells while exerting the antioxidant power to repair skin damage.

### 2.1.3. Microbial Antioxidants

Microorganisms are also important sources of antioxidants, such as actinomycetes, bacteria, cyanobacteria, fungi and lichens. They contain various antioxidants in their own complete antioxidant system, which plays an important role in maintaining their normal life activities [10]. In SKH-1 hairless mice, topical application of the supernatant of milk fermented with *Lactobacillus helveticus* NS8 (NS8-FS) alleviated UVB-induced skin photodamage, including the improvement of the appearance of epidermal thickness, transepidermal water loss and lipid peroxidation levels [42]. Oral administration of *Bifidobacterium breve* in hairless mice can inhibit the increase in UVB-induced hydrogen peroxide formation, protein oxidation and xanthine oxidase activity in the skin [43]. These studies suggest that exploring the effects of microbiological therapy on skin healing and other antioxidant treatments may lead to new strategies.

## 2.2. Artificial Antioxidants

### 2.2.1. Antioxidants Purified by Artificial Extraction

The content of antioxidants in animals and plants is often low. In order to improve the antioxidant effects, antioxidants from animals and plants are often extracted. The extracted product has the characteristics of high safety and strong antioxidant capacity, is easy to be prepared in large quantities and so on. Extraction is the most commonly used method. For example, the extract of watermelon rind is rich in antioxidant substances, which can effectively increase the stability of soybean oil, thereby prolonging its shelf life oil [44].



Ultrasound-assisted extraction (UAE) can be used to extract polyphenolic antioxidants from carotene. Compared with traditional extraction technology, UAE provides higher antioxidant yield and shorter processing time [45].

### 2.2.2. Synthetic Antioxidants

Artificial synthesis is also one of the common ways to obtain antioxidants. At present, there are mainly butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), propyl gallate (PG) and tert-butyl hydroquinone (TBHQ).

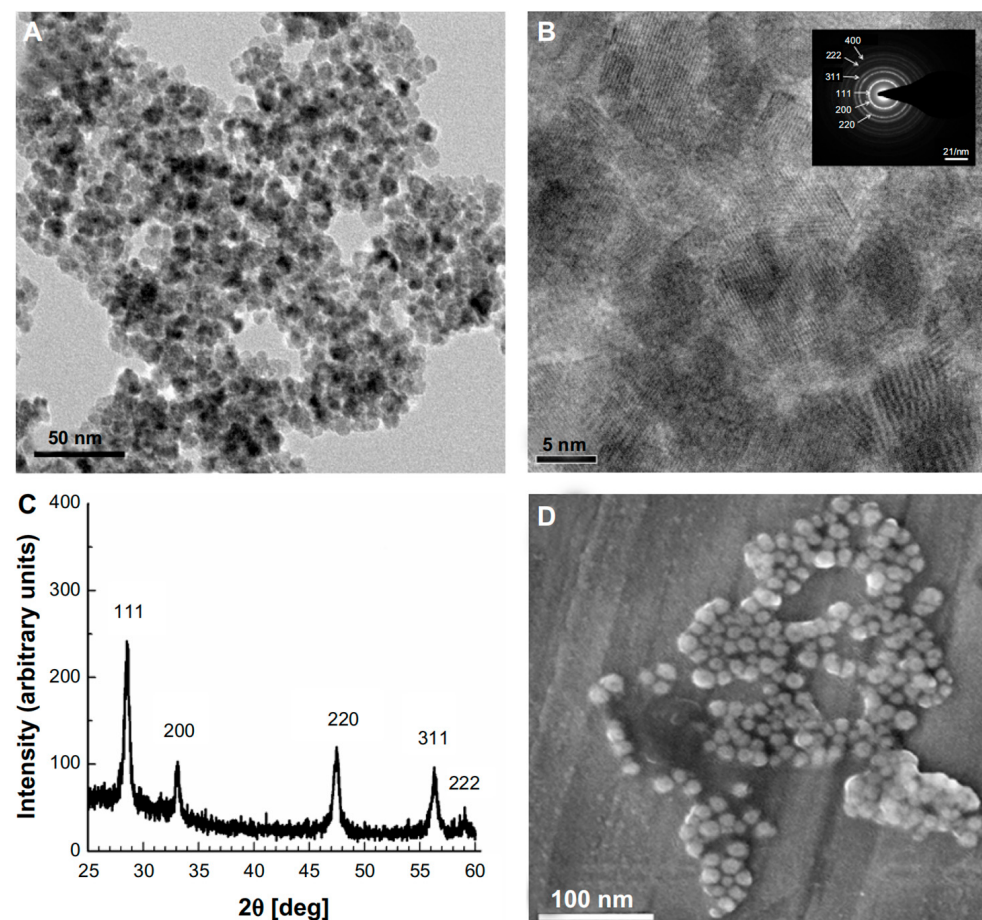
TBHQ is a food-grade phenolic antioxidant. It has been found that TBHQ can antagonize a decrease in arsenic-induced cell viability, the production of ROS and lipid peroxidation, as well as a decrease in superoxide-dismutase (SOD) and catalase (CAT) activities, and improve arsenic-induced intracellular damage and apoptosis [46]. BHA is also a phenolic antioxidant, which can reduce DNA damage and lipid peroxidation induced by mechlorethamine (HN2) and reduce the toxicity of HN2 to A-431 skin cells [47]. N-acetylcysteine, as an antioxidant, can also promote wound healing and has been used as an adjuvant to treat a variety of skin conditions, as well as protect against radiation-induced skin damage, including photoaging, photocarcinogenesis and radiation dermatitis [48].

However, compared with natural antioxidants, synthetic antioxidants have many safety risks, such as excessive use can cause teratogenesis, cancer and some chronic diseases. TBHQ may cause skin irritation in people who are allergic to *Nigella sativa* oil [49] and even in people who are allergic to resins [50]. Adding the antioxidant BHA to the diet of F344 rats resulted in a high incidence of anterior gastric papilloma and squamous cell carcinoma [51]. Propyl gallate is a very effective sunscreen; however, Kahn and Curry [52] reported that it was a strong contact sensitizer. Therefore, the safety evaluation of synthetic antioxidants is very important for their development.

### 2.2.3. Nanoantioxidants

In recent years, nanoantioxidants have gradually become a new trend. Nanomaterials with antioxidant properties have attracted much attention because of their stable structure, renewable activity and antibacterial and antioxidant activity.

The application of nanoparticles in oxidative stress and inflammation can improve the activities of antioxidant enzymes such as SOD and glutathione peroxidase in organisms. At the same time, they can also remove harmful peroxide ions and free radicals in biological cells [53], showing high medical potential in many aspects [54]. There are a variety of nanoparticles. The nanocomposite films prepared on the basis of chitosan and gelatin show good co-persistence and absorption in wound dressings; they not only have good antioxidant capacity but also the capacity to promote wound recovery [55]. A biodegradable hybrid film composed of green synthesized zinc oxide nanoparticles (ZnONPs) and a chitosan (CS) matrix exhibited remarkable antibacterial and antioxidant properties with strong visible emission and UV-blocking activities in the 480 nm region [56]. Nano-enzyme is a kind of nanomaterial with enzyme-mimicking activity, which has relatively high physical and chemical stability in a harsh environment, higher durability and lower cost compared to natural enzymes [57]. Li et al. [58] prepared  $\text{CuCo}_2\text{S}_4$  nano-enzyme, using solvothermal synthesis, which showed excellent peroxidase-like activity under neutral conditions and was proved to have the capacity to accelerate the healing of pH-neutral burn wounds. Cerium oxide nanoparticles (nanoceria) (Figure 3) [59] are a kind of multifunctional enzymes with biocompatibility and a unique biomimetic activity, which can shield UV radiation, protect tissues from UV-oxidation damage and open the way to a smarter and safer reduction in skin damage and cancer caused by UV rays.



**Figure 3.** Characterization of nanoceria. (A) High-resolution transmission electron microscopy (HR-TEM) photomicrograph. (B) HR-TEM micrograph of nanoceria. (C) X-ray diffraction of nanoceria showing the characteristic peaks of the crystal. (D) Scanning electron microscopy analysis showing the spherical shape and homogenous surface topology of nanoparticles [60].

Silver nanoparticles (AgNPs) has attracted much attention in the field of biomedicine because of their anti-inflammatory, bacteriostatic, antioxidant and wound-healing capacities. One study [61] found that the biocompatible AgNPs synthesized from antioxidant-rich aqueous extract of *Aerva javanica* had good antioxidant potential, promoted rapid wound healing after adding it to a hydrogel and showed low toxicity in vitro and in vivo. As one of the important metal oxidation nanomaterials, zinc oxide nanoparticles (ZnONPs) are widely used in the biomedical field because of their ultraviolet-absorbing, antibacterial, anti-inflammatory and other properties. The green synthesis of ZnONPs from the aqueous extract of sea lavender showed effective antibacterial and antifungal activities, as well as considerable antioxidant potential [62].

However, many experiments have shown that metal nanoparticles can pass through the skin and enter the body. After the external application of nano-silver dressing on a burn wound, silver nanoparticles can enter the blood through the damaged skin and accumulate in the body to cause liver and kidney toxicity [63]. Moreover, ZnONPs and TiO<sub>2</sub>NPs can enhance DNA oxidative damage by increasing the production of ROS, causing concerns about the safety of ZnONPs and TiO<sub>2</sub>NPs [64]. Therefore, exploring how to reduce the toxicity of metal nanomaterials and increase their biosafety has become a new development of and strategy for the application of metal nanomaterials in the field of biomedicine.

#### 2.2.4. Gaseous Antioxidants

As an antioxidant gas, H<sub>2</sub>S can resist oxidative substances such as reactive oxygen species (ROS) and reactive nitrogen species (RNS) and protect skin from oxidative stress. [65]. It has been found that NaHS can promote the migration of skin fibroblasts and keratinocytes by alleviating ROS and increasing mitochondrial membrane potential, indicating that H<sub>2</sub>S can promote skin repair through antioxidation [66].

Hydrogen has been widely researched in recent years, and more and more studies find that hydrogen has the effects of antioxidation, anti-inflammation, anti-apoptosis and so on. As a small molecular substance, hydrogen can easily pass through membrane structures, quickly reach the damage site, react with the highly oxidizing ROS and scavenge oxidation products such as free radicals [67]. Hydrogen can also enhance the antioxidant capacity of peroxidase, thus reducing the damage of oxidative ions such as ROS [68]. A Japanese study [69] showed that for hospitalized elderly patients with severe stress ulcers, the intake of hydrogen-rich water through tube feeding can achieve wound size reduction and early recovery, which might be related to the construction of type I collagen in skin fibroblasts or the enhancement of mitochondrial reduction and ROS inhibition in epidermal keratinocytes. Another study [70] showed that inhaling H<sub>2</sub> can significantly reduce wound area, 8-oxo-dG level (oxidative DNA damage) and apoptosis rate in skin injuries. Zhao et al. [71] found that hydrogen-rich water can significantly improve the survival of a skin flap after ischemia and reperfusion and reduce the ischemia–reperfusion injury, leukocyte infiltration and the production of lipid peroxides and inflammatory cytokines. Hydrogen has been widely studied and explored, and it plays a variety of physiological roles in skin injury repair.

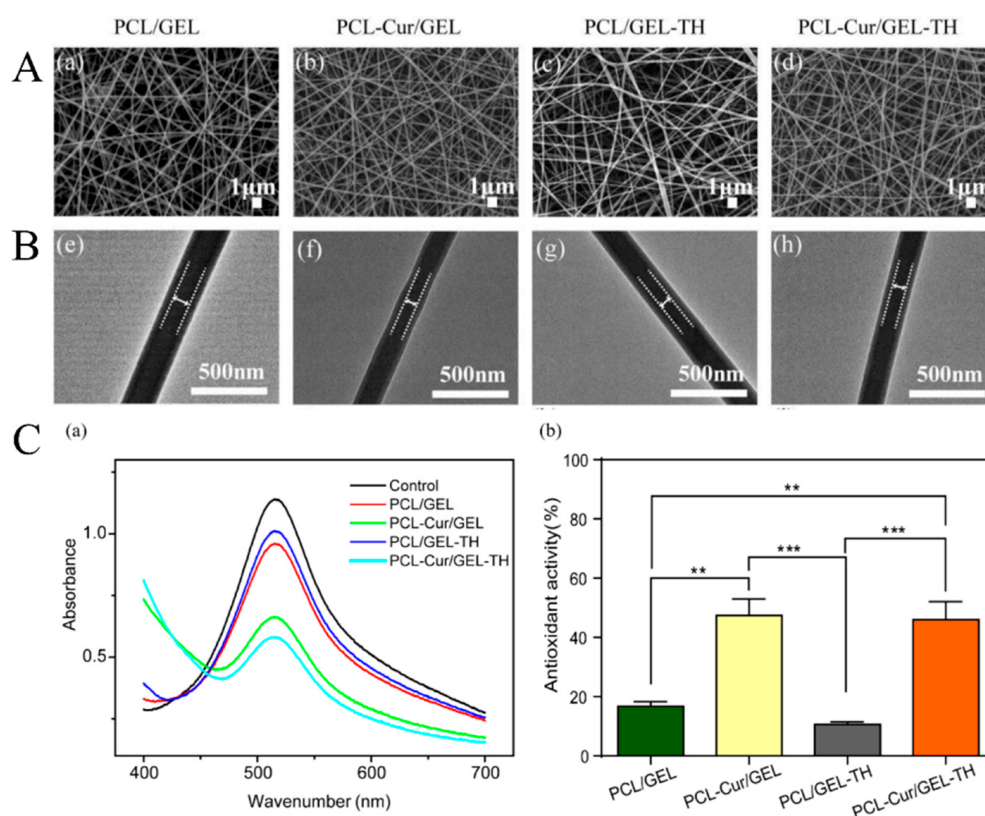
### 3. Antioxidant Carriers

Drug carriers can change the way drugs enter and are distributed in the body, control the speed of drug release and deliver drugs to the targeted organ system so as to improve the utilization, safety and effectiveness of drugs. The main carriers of antioxidants used for skin repair are electrospun nanofibers, nanoemulsions, microemulsions, nanoliposomes, hydrogels and so on.

#### 3.1. Electrospun Nanofibers

Among different nanomaterials, nanofibers prepared by electrospinning are widely used in the best finishing materials because of their excellent physical and mechanical properties. By adjusting the arrangement of nanofibers, the controlled release of loaded drugs and superior mechanical properties adapted to limb movements can be realized [72]. Porous nanofiber mats readily produced by the electrospinning process offer a promising solution in the management of wounds [73].

Various polymers can be selected for electrospinning materials according to the specific requirements of damaged skin [72]. Brahatheeswaran et al. [74] prepared fiber membranes by electrospinning zein fibers in TFE solutions containing curcumin at a constant flow rate of 1.0 mL h<sup>−1</sup> under the electrostatic field strength of 2.0 kV cm<sup>−1</sup>, which had good cell adhesion and proliferation, strong antioxidation and good sustained-release effects and can be used in wound dressing and as drug carriers. Dan et al. [75] loaded curcumin (Cur) into a polycaprolactone (PCL) core and broad-spectrum antibacterial tetracycline hydrochloride (TH) into a gelatin (GEL) shell and prepared a PCL–Cur/GEL–TH core–shell nanofiber membrane using coaxial electrospinning. The membrane showed good antioxidant activity, excellent antibacterial activity, good water absorption capacity and hydrophilic and mechanical properties and had great potential to promote wound repair (Figure 4). Li et al. [76] successfully created a wound dressing core–shell nanofiber membrane (PGEC: poly(L-Lactic-co-caprolactone) (PLCL), gelatin and epigallocatechin-3-O-gallate (EGCG)) using a coaxial electrospinning technology, which improved the low bioavailability of EGCG in vivo, had excellent biocompatibility, good antibacterial and antioxidant capacities, can slow the release of drugs and promote wound regeneration and healing.



**Figure 4.** (A) (a–d) SEM images. (B) (e–h) TEM images. The white dash line in (B) (e–h) indicates the border between the PCL core and the GEL shell. (C) (a) Absorbance of DPPH solution with different nanofibrous membranes; (C) (b) DPPH-scavenging activities of different nanofiber membranes; \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$  [75].

In summary, based on electrospinning loading technology, nanoparticles and bioactive substances can interact with the electrospun film components and improve the performance of drug delivery.

### 3.2. Microemulsions and Nanoemulsions

Microemulsions are usually composed of an oil phase, a surfactant, a cosurfactant and an aqueous phase and have optical transparency, thermodynamic stability and low interfacial tension, which can enable the effective dissolution and higher bioavailability of the drug [77]. Resveratrol is a particularly effective antioxidant with anti-inflammatory and anti-proliferative properties [78]. It has been found that a microemulsion composed of sucrose oleate (SO), ethanol, isopropyl myristate (IPM) and water (MESO-E) shows a significant increase in the amount of resveratrol incorporated into the skin, making it an effective delivery carrier of resveratrol for the skin [79]. However, because microemulsions contain a large amounts of surfactants and cosurfactants, they may be irritating to the skin and have not been widely used in skin repair.

Nanoemulsions are colloidal systems formed by mixing oil, emulsifier and water, which are dynamically stable and thermodynamically unstable and are divided into oil-in-water (O/W) and water-in-oil (W/O) systems, of which oil-in-water nanoemulsions are the most commonly used [80]. As traditional drug carriers, nanoemulsions are not only simple to prepare but also can cooperate with drugs to achieve a safer, more stable and more significant drug-use effect. It was found that an optimized curcumin-encapsulated  $\alpha$ -tocopherol nanoemulsion system, obtained by adjusting the content of ingredients in the formulation and using a high-speed homogenization technique, can significantly reduce oxidative stress, enhance collagen deposition, prevent wound bacterial contamination and accelerate the process of skin tissue regeneration [81]. Sunflower oil contains vitamin E



which can be used as a natural sunscreen to absorb the UVB light. One study found that sunflower oil nanoemulsions prepared by a self-emulsifying method with F3 (Tween 180%, sorbitol 38%), F22 (Tween 280%, sorbitol 36%) and F24 (Tween 380%, sorbitol 34%) and 26% of sunflower oil as sunscreen substances had a higher SPF value and can be considered more effective when used in sunscreen cosmetics [82].

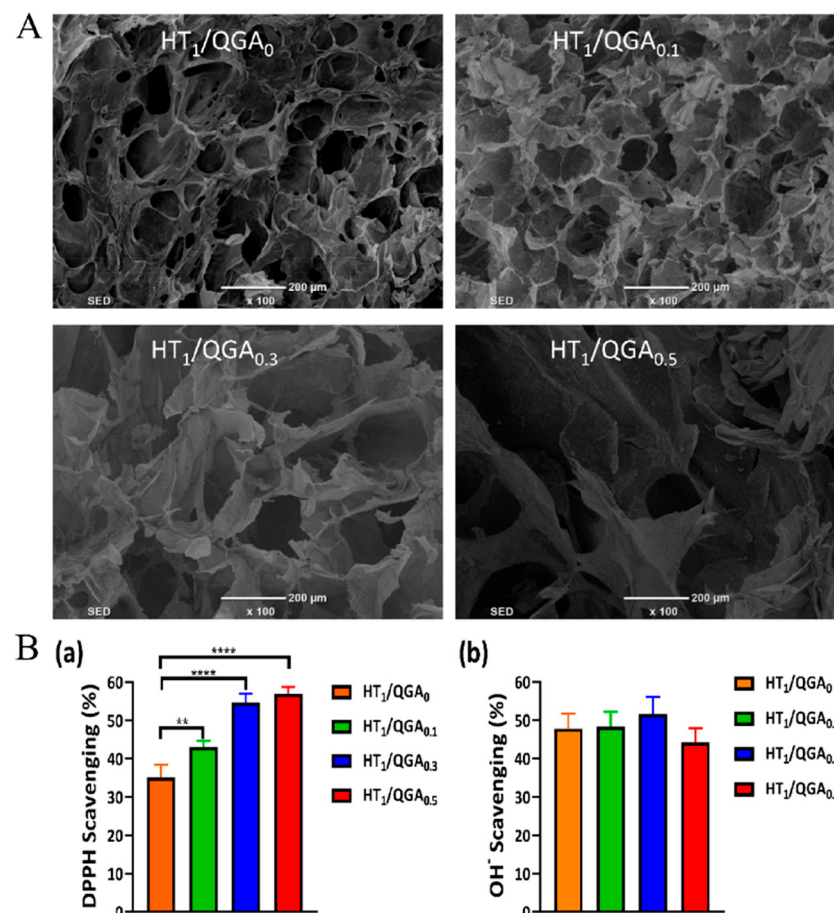
### 3.3. Nanoliposomes

Nanoliposomes are liposome structures with a particle size smaller than 100 nm. They have the special effect of nanoparticles in terms of stability, absorption and distribution in vivo. They can carry drugs directly to the target tissue to play a pharmacological role. The seeds of moringa tree (*Moringa oleifera* Lam.) are rich in isothiocyanates (MITC), which have excellent antibacterial, anti-inflammatory, antioxidant and antitumor activities [83]. It was found that amphiphilic hyaluronic acid (HA) coupled with ceramides (CEs) was used to modify MITC nanoliposomes by a thin-film hydration method to prepare HACE/MITC nanoparticles (NPs), which can significantly increase the activity of antioxidant enzymes, eliminate ROS induced by UVB and reduce the expression of MMP-1, MMP-3 and MMP-9 caused by radiation-induced photoaging [84]. Anthocyanins are easily degraded under the conditions of high pH value, light, heat and oxygen. A large number of studies have shown that nanoliposomes improve the stability, bioavailability and biological activity of anthocyanins [85]. One study [86] found that a combination of propylene glycol liposomes and silver nanoparticles from grape extract prepared using a new optimized one-step green preparation method with castor seed as a raw material can effectively eliminate several pathogenic microorganisms and dangerous free radicals and protect fibroblasts and keratinocytes against antioxidant stress, thus providing a suitable formula for local treatment of skin injuries.

### 3.4. Hydrogels

Hydrogels are a new type of dressing to prevent secondary wound injury and infection. Hydrogels attract more and more attention because of their adjustable chemical, physical and biological properties and three-dimensional cross-linked polymer networks that can absorb and retain large amounts of water [87]. One study [88] found that a hydrogel prepared using MnO<sub>2</sub> nanosheets (EM) coated with  $\epsilon$ -polylysine (EPL) and insulin-loaded self-assembled aldehyde Pluronic F127 (FCHO) micelles showed strong antioxidant activity in the application in chronic wounds. Another study [89] found that a AgNP-PADM hydrogel synthesized by embedding AgNPs into a PADM hydrogel can slowly release AgNPs, which showed sufficient antibacterial and antioxidant properties, negligible toxicity and can promote angiogenesis and cure skin defects. Silver nanoparticles containing chitosan–polyethylene glycol (PEG) pre-polymer solution were synthesized by reducing silver nitrate with a polyethylene glycol and chitosan solution to convert silver ions into silver nanoparticles. A chitosan–PEG hydrogel impregnated with silver nanoparticles, which were formed by crosslinking the obtained pre-polymer solution with glutaraldehyde, also improved the antibacterial and antioxidant properties and promoted the healing of diabetic wounds [90]. Yikun Ren et al. [91] prepared and characterized tyramine-grafted and hyaluronic-acid/gallic-acid-grafted quaternized chitosan (HT/QGA) hydrogels with injection and antioxidant properties, which showed excellent injectability, good antioxidant activity and biocompatibility with great potential application prospects in wound healing (Figure 5).





**Figure 5.** (A) The morphology of HT/QGA measured by SEM. (B) Antioxidant efficiency of HT/QGA hydrogel: (a) DPPH-radical- and (b) hydroxyl-radical-scavenging activities in hydrogel; \*\*  $p < 0.01$ , \*\*\*\*  $p < 0.0001$ , mean  $\pm$  SD,  $n = 3$  [91].

#### 4. Conclusions

Many chronic diseases of human body are closely related to the imbalance of the reduction–oxidation reaction. Rational utilization and development of new antioxidants play an important role in human health. In this paper, the sources of antioxidants and the carriers that can realize drug release are summarized and analyzed in order to provide guidance for the development of new nanoantioxidants and research on new skin repair systems.

Natural antioxidants, a natural resource, have been proved to have strong antioxidant effects. Artificial antioxidants are also widely used because of their strong antioxidant capacity and easy mass preparation, especially the nanomaterial with antioxidant properties. They have attracted much attention because of their stable structure and renewable activity and gradually become a new trend. Gas antioxidants have also been found to play a variety of physiological roles in the repair of skin injuries. Drug carriers such as electrospun nanofibers, nanoemulsions, microemulsions, nanoliposomes and hydrogels have also been explored to improve the utilization, safety and effectiveness of antioxidants. However, there are still some deficiencies in the exploration of antioxidants, and more safety data are still needed in order to provide the experimental basis and confidence for the subsequent study of new strategies for skin damage repair and the promotion and application of new drug-carrier structures. Future studies should strive to find the most suitable antioxidants and their carriers in various fields and maximize their advantages in promoting the repair of skin damage and maintaining human health.

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