Quantum Dots

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Quantum dots (QDs) are an advanced nanomaterial technology deem to be useful in clinical and biomedical applications. QDs have given a big impact in biomedical application due to their imaging potential which significantly improved the clinical diagnostics test. Meanwhile, QDs also have the potential to become the nanocarrier for the drug.

Keywords: quantum dots ; nanotechnology ; wound healing

1. Characteristics of Quantum Dots

Quantum Dots (QDs) were first discovered by Ekimov and Onushenko in 1981, and are nanoscale semiconductor crystals and first nanotechnologies to be applied in biological science made of heavy metals [1][2]. QDs have shown great potential in several biomedical types of research including fluorescence imaging, disease detection, fluorescence assays for single protein track, drug discovery and intracellular reporting due to their mechanical and physicochemical properties [3]. QDs have five distinct properties that ameliorate tremendous research interest including (1) the nano size ranges from 4 until 12 nm in diameter, (2) narrow and size-tunable Gaussian emission spectra which excite to the near-infrared (NIR); lower than 650 nm, (3) self-luminescence due to their absorption extinction coefficients and high fluorescence quantum yields, (4) QDs are photochemically robust due to its inorganic composition and the fluorescence intermittency with observation of single dot event, (5) observing a single protein compound [4].

The synthesis of QDs results in organic capping ligands that make them biocompatible, and a biological targeting development which achieved by surface modification and linking with antibodies, peptides or small molecules [4][5]. QDs also have been applied in biomedical applications such as delivery of drug, bio-sensing and also tissue engineering [6]. QDs are ideal nano-carriers for the drug due to their high surface area to interact with other molecules especially their strong interactions with organic molecules and specific compounds [7]. Application of QDs in drug delivery has increased drug stability, prolonged in vivo circulation time, improve the distribution and metabolism process of drugs and enhance absorption [3]. The optical properties of QDs have been used for bio-imaging applications in various biological research for deep-tissue imaging with reduced light scattering and low tissue absorption [8]. Researchers worldwide used the QDs as fluorescence labeling for both in vivo cellular imaging and in vitro assay detection due to photoluminescence properties [9].

There have been increasing research on QDs in wound healing as these nanoparticles equip the same properties as their bulk counterparts and more stable due to their large surface area [10]. The unique physicochemical characteristics of QDs are highly beneficial in tissue engineering applications especially their antibacterial properties as these aspects are important in development of biomaterials. QDs also can enhance the mechanical strength of tissue scaffolds and hydrogels for wound healing, or for regenerative medicine [11]. Due to its nano-scale size (less than 20 nm), QDs have low toxicity towards the cells and have enzymatic functions such as oxidase which make it suitable to be incorporated into a bioscaffold [12]. The large surface area of QDs could bind to the ligands which involved in wound healing process. For example, carbon quantum dots proven to involve in angiogenesis process as these nanoparticles able to enhance the anti-angiogenic factors expression which is crucial to avoid overexpression of pro-angiogenic factors expression [13]. QDs also involve in signaling pathway which enhance the inflammation phase of wound healing as it increases the interleukin-6 expression [14].

2. Wound Healing Properties of QDs

The outcomes from the review highlighted the advantageous of quantum dots (QDs) in wound healing. There are various reports on the application of QDs in wound healing and it has been tested in vivo, in vitro and in ovo model. The overall result of QDs seems to be beneficial towards wound healing as the treatment group obtains better results compared to the control group. However, the combination of QDs with polymer e.g., carbon quantum dots with hybrid tannic acid and keratin (CQDs-TA/KA) hydrogel yields a more appealing result compared to QDs itself [15].

2.1. Wound Closure

The *in vivo* studies were used to study the biological effect of QDs in a dynamic and complex biosystem e.g., the wound closure. Apart from having QDs derived from various types of heavy metals, the papers were primary aim to assess their biological effect in selected wound model in each study. Most of the studies inflict a cutaneous incisional wound and there only one study that inflicts burn wound on the animal. The wound healing assessments were performed by gross morphology of the wound, the size of wounds and the histological evaluation using hematoxylin and eosin (H & E) staining to determine the condition of the regenerated tissue [16]. The in vivo studies reporting the effects of QDs on wound healing were simplified in Table 1.

Table 1. In vivo study on wound healing.

No.	Experimental Model	Type of Quantum Dots	Outcome Measures	Results	Conclusion
1	Sprague-Dawley rats 6 weeks old Weight 200 g Excision wound (1.00 cm^2)	VO_xNDs	1. Morphology of wound 2. Histological evaluation (H & E stain)	H_2O_2/ VO_xNDs have 60% decrease in wound area compared to control and rigid epidermal layer after 6 days therapy	H_2O_2/VO_xNDs group have the greatest wound healing capacity among all tested group
2	Sprague-Dawley rats Weight 250 ± 20 g Full thickness wound (1.80 cm^2)	NCQDs	1. Wound morphology 2. Histological evaluation (H & E stain) 3. White blood count (blood slide)	Treatment with NCQDs have significantly higher healing rate where the wound area is 0.2% at the 14th day of treatment and lower white blood count which is 1×10^{10} L^{-1} indicate decrease of inflammation in wound area	NCQDs show effective treatment towards wound healing
3	Albino Wistar rats Weights 150–200 g Excision wound (3.14 cm^2)	CND	1. Morphology evaluation 2. Histological examination (H & E stain)	Treatment of OCNDs had more than 80% of healing compare to control (65%) and shown to have intact dermal and epidermal structure which does not show signs of inflammation nor infection	Topical application of OCNDs improved the wound healing process
4	Wistar rats Burn wound	GQDs	1. Morphology study of recovery process 2. Histological assessment (H & E stain and Masson's trichrome staining)	Treatment group have higher healing rate than control group and formation of fibroblasts are 10% higher than control	GQDs able to accelerate the repair of skin lesion in burn wound healing model
5	Rats 10–12 weeks old Weight 250–300 g Full thickness wound (1.50 cm^2)	GOQDs	1. Gross morphology of wound 2. Histological assessment (H & E stain)	Treatment with TA/KA-GOQDs show 98% of wound are closure and matured epidermal layer after 16 days of treatment	TA/KA-GOQDs proves its ability to treat wounds within short period of time and without side effects
6	Rats Incision wound	CQDs	1. Gross morphology of wound 2. Histological assessment (H & E stain and Masson's trichrome staining)	DFT-C/ZnO-hydrogel-treated group have 95.7% of wound closure by 10 days of treatment. H & E staining show that this treatment group have complete epidermal structure in 2 days Dense collagen fiber have been observed in treatment group after 10th day of treatment	Treatment with DFT-C/ZnO-hydrogel groups exhibit the best wound healing results
7	Rat Weights 260 g Excision wound (1.00 cm^2)	CND	1. Morphology evaluation	The wound heals at ~100% at 16th days in with CDs/chitosan nanocomposite compared to 40% of control group	The characteristic of CDs/chitosan shown to be beneficial as wound dressing products

No.	Experimental Model	Type of Quantum Dots	Outcome Measures	Results	Conclusion
8	BALB/c mice 8 weeks old Incision wound	MoS_2QDs	1. Morphology evaluation	The infected wounds almost 90% completely healed in photoexcited MoS_2QDs group, compared to control group	The potential application of the of MoS2 QDs was demonstrated great improvement of wound healing
9	Female BALB/c mice 8 weeks old Weight 18–23 g Excision wound (0.78 cm^2)	MoS_2NF	1. Gross morphology of wound 2. Histological assessment (H & E stain and Masson's trichrome stain)	The treatment groups show formation of epidermal layer for wound closure at 5th day of treatment and attachment of collagen fiber with dermal layer	The MoS_2NF shown improvement of wound healing in short period of time
10	Male Kunming mice 6–8 weeks old Weight 180–220 g Excision wound (0.04 cm^2)	GQDs	1. Gross morphology of wound	Treatment with H_2O_2 and GQD band aid groups shows no significant results in wound closure	Treatment with GQD band aid groups as wound dressing shows no significant result for wound healing
11	Male mice 6–8 weeks old Weight 180–220 g Incision wound (1.6 cm^2)	CQDs	1. Gross morphology of wound 2. Histological assessment (H & E stain)	CQDs-treated group show complete closure of wound and higher degree of healing within 5 days of treatment	CDQs contribute to faster wound healing and great potential for wound dressing
12	Male mice Excision wound (0.79 cm^2)	ZnOQDs	1. Morphology assessment	Treatment of ZnOQDs with GO-CS hydrogel shown 90% of wound closure after 14th day of treatment	ZnOQDs imbedded in GO-CS hydrogel show potential to be used for wound dressing

Based on the results obtained, the QDs supports the wound healing process in vivo. The histological assessment shows the regeneration of tissue and formation of blood vessel when treated with QDs. Xiang et al., 2019 show even disposition of collagen and dense collagen fibers when treated with QDs [17]. Haghshenas et al., 2019 show that QDs involve the formation or regeneration of tissue at the wound site are faster in treated compare with non-treated model [18]. In the context of wound healing, progression in the inflammatory stage depends on the suitable microenvironment at the wound site. Infection is also one of the factors which affect the healing process where it is important for the removal of micro-organisms before advancing to the next stage of wound healing process [19]. Microbial infections may prolong the inflammatory stage and causing high expression of pro-inflammatory cytokines (interleukin 1 alpha, interleukin 1 beta and tumor necrosis factor alpha) that not only harmful towards infected cells but also healthy cells [20].

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