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Drug-laden 3D biodegradable label using QR code for anti-counterfeiting of drugs

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ABSTRACT

Wiping out counterfeit drugs is a great task for public health care around the world. The boost of these drugs makes treatment to become potentially harmful or even lethal. In this paper, biodegradable drug-laden QR code label for anti-counterfeiting of drugs is proposed that can provide the non-fluorescence recognition and high capacity. It is fabricated by the laser cutting to achieve the roughness over different surface which causes the difference in the gray levels on the translucent material the QR code pattern, and the micro mold process to obtain the drug-laden biodegradable label. We screened biomaterials presenting the relevant conditions and further requirements of the package. The drug-laden microlabel is on the surface of the troches or the bottom of the capsule and can be read by a simple smartphone QR code reader application. Labeling the pill directly and decoding the information successfully means more convenient and simple operation with non-fluorescence and high capacity in contrast to the traditional methods.

1. Introduction

With the rapid development of pharmaceutical industry, counterfeit products have emerged in the field of medical science. Fake drugs bring about an enormous damage, not only destroying the health and consumer-finances, but also decreasing public's trust of government facility system and sales revenue of the pharmaceutical companies, even condoning more criminal behaviors. According to the world health organization (WHO) and the United Nations Office (UNO on Drugs and Crime), worldwide counterfeits account of nearly 10%, with a higher proportion in sub-Saharan African and Southeast Asian regions. [1–3]The counterfeit market annual trade volume reaches $7.5 billion, rising by almost 90% in 5 years [4], with over $16,680,000 fake drugs being intercepted in 2011 by the US Customs and Border Protection (CBP) [5]. Although $400 million has been injected into the West African anti-malarial market, so far [6], fake meningitis vaccine took 2500 people's lives in Niger, of which 64% were forged [7,8]. Furthermore, numbers of people were killed due to illegal channels of mixing up cough medicine and drugs with diethylene glycol in Niger, 2008 [9,10].

Apart from security power and the rules of law, we should concentrate more on the anti-counterfeiting technology. Radio Frequency Identification (RFID) is a wireless use of electromagnetic fields to transfer data, for the purpose of automatically identifying and tracking the tags attached to objects, which was firstly applied during the establishment of the drug supply chain, 1996 [11]. It is reported that Pfizer initially used RFID tags for the security of bottled medicines in 2005. [12] But during the RFID system pilot project, the US Food and Drug Administration (FDA) found that there were some problems in its applications, such as it influences the quality, safety and efficacy, and in addition to its flaw by technical standards in its accuracy of identification through various processes. Unmatched frequency could cause interference and insufficiency of the readable distance [13,14]. Pharmaceutical packaging technology is the alternative solution, which includes fluorescent inks, watermarks, and micro-printing, through which it's still hard to escape from the doom of counterfeit criminals' [15], for various reasons of uncomplicated measures and materials [16]. Although printing anti-counterfeiting codes on the pharmaceutical package or blister card is possible and applicable, replacing them with fake ones is still a piece of cake for criminals. Besides that, fingerprint-like encoding strategies [17,18], organic electronic devices [19], nanopillar array paper [20], 3D microstructure films [21], and invisible photonic printings [22] can make their ways into anti-counterfeiting authentication.

Encoding polymer microparticles [23] and luminescent QR codes [24] are attractive as information carriers. Even DNA codes can be scanned directly by a smartphone [25]. Sunghoon Kwon and Wook Park's team from Kyung Hee University attempted to introduce lithographically encoded polymer microtaggants into capsules, which significantly improved the efforts to combat counterfeiting compared with the traditional methods [26]. However, this micro polymer was mixed with a fluorescent acrylic monomer, methacryloxyethyl thiocarbamoyl rhodamine B, which further complicates the fabrication in materials, as well as the identification under a fluorescence microscope. Furthermore, the approach that microtaggants are still required to be taken out of capsules, which means separating drugs and codes, seems not

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rigorous enough to come to terms of anti-counterfeiting. Also it is obviously inconvenient and costly for most public consumers.

Since counterfeit drugs pose a growing threat to our live because they can deliver hazardous treatment or even cause death, we propose an encoded three dimensional drug-laden biodegradable label without fluorescence labeling for anti-counterfeiting of drugs. The technologies include the process of laser etching [27], micro machining and micro molding, as well as the designing and arrangement of identification. The experiments for screening of biodegradable material have been conducted, ensuring the safety of the drug labels. Using high-capacity and error-correctable QR code makes point-of-care testing convenient with smartphones. The developing ways of pharmaceutical packaging and storage are further discussed in this paper, which are being planned for further research.

2. Materials and methods

2.1. Materials and devices

Polymethyl methacrylate (PMMA) sheets (2.0 mm thick) were purchased from Sunjin Electronics Co., Ltd. (Taiwan, China). Polydimethylsiloxane (PDMS) was purchased from Dow Corning Co., Ltd. (Midland, MI, USA). Polyvinyl alcohol (PVA) including 30,000 – 70,000 MW and 80,000 – 124,000 MW were purchased from Sigma-Aldrich Co., Ltd. (St. Louis, MO, USA). Hyaluronic acid (HA) including 400,000 – 1,000,000 MW and 1,800,000 – 2,200,000 MW were purchased from Shanghai Jiao Yuan Industry Co., Ltd. (Shanghai, China). Pharmaceutical gelatin (PG) including 50,000 – 60,000 MW and 150,000 – 250,000 MW were purchased from Aladdin Industrial Co., Ltd. (Shanghai, China). Laser cutting system (speedy 100) was purchased from Trobec Co., Ltd. (Wels, Austria). Vacuum pump and oven were purchased from Shanghai Boxun Industry & Commerce Co., Ltd. (Shanghai, China). An iPhone 5 (Apple Inc., Cupertino, CA, USA) was also used.

2.2. Design and fabrication of drug-laden biomaterial label with QR code

The QR code has high-capacity and error-correctability, and also has comprehensive reading and fast generational abilities. A traditional bar code only enables to carry 12 to 20 characters [28], which is inadequate for drug security.

To obtain the drug-laden QR code label, it is indispensable to prepare the encoding mold. We attempted to adopt PMMA plastic as the mold on account of its excellent transparency, insulative resistance, aging resistance, corrosive resistance, easy processing, light weight and other good characteristics. Firstly, we need to require a QR code carrying production information, such as the drug name, manufacturer and its expiry date, through a two-dimensional code generator from a common website. In our laser cutting system, the light propagates along the vertical direction and spreads horizontally when the image plane is engraved over the PMMA sheet by a commercial software (Job control, Trobec Inc.), which is applicable for industrial production with high efficiency (Fig. 1a). Before laser engraving, the 2.0 mm thick PMMA sheet was ultrasonically washed for 10 min in deionized water, and then rinsed by a lot of distilled water to remove minor impurities attached to its surface. After drying it with compressed nitrogen, the desired template is engraved on the platform under the following conditions: laser energy density of 7.26 J/cm^2, infrared wavelength of 10.6 μm and the maximum power of 1300 W. Focal distance from the substrate surface was maintained at 61.64 mm, under the processing speed of 180–280 cm/s. The pattern of the template size was designed according to a commercial software (AutoCAD 2012, Autodesk Inc.) which was 4.35 mm long × 4.35 mm wide × 2.0 mm thick, with power of 12.66 W and its pace 189 cm/s. The laser parameters which are highly relevant with the clarity of QR code would be analyzed later in the results.

Secondly, the code patterns are planned to be replicated from PMMA sheets to biocompatible materials (Fig. 1b). The liquid PDMS is cast over the patterned PMMA, and cured under oven with 70 °C for 1.5 h. The PDMS replica with QR code functional microstructures was removed from the PMMA master. The biomaterials, which we selected to make the drug capsule, were cast over PDMS mold with microstructures and allowed to dry in room temperature, and were removed from the PDMS mold. Another package was that the drug pill with QR code. We used the biomaterials to mix with drug content, and the mixed solution was cast over the PDMS mold with QR code. Then, the drug carrying QR code label was obtained after separation with the PDMS mold.

We selected three kinds of materials (HA, PG and PVA) consisting of different molecular weight owning to their good biocompatibility, degradability and edibility. There were solutions including 1 wt.% HA, 10 wt.% PG and 15 wt.% PVA prepared for further use. These solutions were separately dropped over the PDMS mold with a pipette then ventilated them at room temperature (25 °C) for 1 day. Obviously increasing the temperature and more ventilation can be effective to decrease the time of solidification. After polymerization, three polymers were

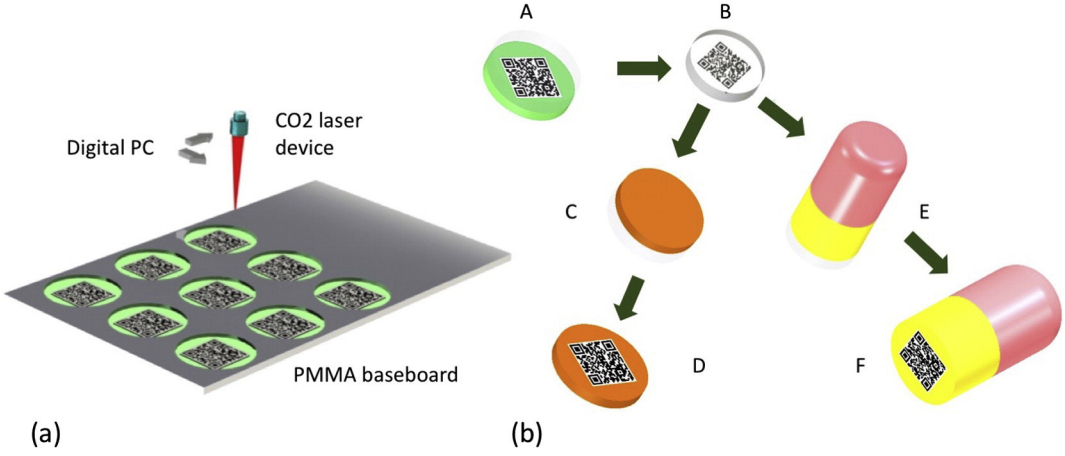

Fig. 1. Design and fabrication processing of drug-laden biodegradable label. (a) Schematic diagram of the process of engraving QR codes over PMMA. (b) Schematic diagram of the micro mold processing of the drug-laden biodegradable label. The code patterns are replicated from PMMA sheets to biocompatible materials. The "A" represents encoded PMMA is poured by a layer of PDMS, then the PDMS is peeled off after drying and we get the "B" which is a replica of PDMS mold with QR code functional microstructure. The "C" means the biomaterials are poured over the "B" and produces the label film "D"; the "E" is a cylindrically shaped process over B and results into a capsule F.