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Solventless visible light-curable coating: I. Critical formulation and processing parameters

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ABSTRACT

Film coating is generally accomplished by spraying polymers dissolved in solvents onto a cascading bed of tablets. The limitations associated with the use of solvents (both aqueous and organic) can be overcome by the use of solventless coating technologies. In this proposed solventless photocurable film coating system, each layer of coating onto the pellets (non-pareil beads) was formed using liquid photocurable monomer, powdered pore-forming agents, photosensitizers and photoinitiators in a mini-coating pan and later cured by visible light. Yield, coating efficiency, variation in color, diameter and roundness were determined for each batch to evaluate process efficiency and coating quality. It was found that the ratio (S/L ratio) of the amount of solid (S) pore-forming agent to volume of liquid (L) monomer, particle size and type of the pore-forming agent, concentration of initiator, and total exposure (light intensity × exposure time) of light were critical formulation and processing parameters for the process. Using lactose as a pore-forming agent, an optimum ratio of pore-forming agent to photocurable polymer was 1.8–3.0 to achieve good process efficiency and uniformity. The ratio was sensitive to particle size and type of pore-forming agent.

1. Introduction

Film coatings are often applied to drug particles, drug loaded pellets, tablets and capsules to provide modified or delayed release characteristics (Porter, 1982). However, there are several disadvantages associated with organic (toxicity, flammability, higher cost) and aqueous (use of heat and water) based coatings. In response to the issues associated with the use of solvents including water, several solventless coating techniques are being investigated. Compression coating (or dry coating or press-coating) (Ozeki et al., 2004), hot-melt coating (Achanta et al., 1997; Kennedy, 1995), super-critical fluid coating (Thies et al., 2003; Tom and Debenedetti, 1991), dry powder coating electrostatic coating (Grosvenor, 1991) and photocuring are the primary methods being investigated for solventless pharmaceutical coating (Bose and Bogner, 2007).

Photocuring is an alternative solventless coating method that often involves a free-radical polymerization reaction. Functional moieties on the liquid photocurable materials react to form a solid crosslinked network. The photocuring system has three major components: a light source, specially functionalized liquid prepolymer or monomers, photoinitiator and/or photosensitizer (Pappas, 1985). Photocurable systems are usually purged with nitrogen to reduce the presence of oxygen which can slow down and/or reduce the extent of curing in acrylate or methacrylate terminated prepolymer/monomer systems by acting as a scavenger in free-radical reaction (Decker et al., 1980) and also by quenching excited states. Among the photocurable materials that have been studied, acrylate or methacrylate-functional prepolymers and monomers are the most widely used (Otsubo et al., 1984).

Photocuring has wide application in the paint, adhesive and photo-imaging industries (Roffey, 1982, 1986, 1998) as well as in the dental and medical fields (Kurze, 1994), specifically in composite dental filling (Lovell et al., 2001; Tanoue et al., 1998), preventive treatment for caries (Wilder et al., 1999, 1983), assembly of medical devices (Burger, 2000), and wound dressing (Lee et al., 1992; Szycher et al., 1985, 1986a, 1986b; Trotter, 2002). However, the pharmaceutical industry has yet to use photocuring in commercial applications. Savage and Clevenger explored the use of water-soluble photocurable polymer systems for coating pharmaceutical dosage forms using visible or ultra violet light. Their process included the aqueous coating of hydroxyethyl methacrylate and subsequent photocuring (Savage and Clevenger, 1996a, b). Solventless photocuring was previously investigated for phar-

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maceutical coating. Ultraviolet light was used to cure derivatized silicone polymer films on pellets or non-pareil beads in small scale coating equipment; coatings of sufficient integrity were obtained (Wang and Bogner, 1995). However, the silicone films formed a complete and almost perfect barrier to drug diffusion. In an extension of that work, functional photocurable coatings were applied by incorporating different powdered pore-forming agents to the photocured silicone coating matrix. That process involved UV light to cure the acrylate terminated siloxanes (Bose and Bogner, 2006). The yield and process efficiency of the photocurable coating system were 95% and 85%, respectively. The type, particle size and level of the pore-forming agents in the coating as well as the intensity and time of exposure to UV light and initiator concentration were found to be critical for the process (Bose and Bogner, 2006). These parameters were optimized to minimize intra-batch and inter-batch variation of the process.

While the UV photocured coating of siloxane systems was shown to be successful, the toxicity profiles of those siloxanes is unknown at this time. Tetraethyleneglycol dimethacrylate (TEGDMA) and bisphenol A-glycidyl methacrylate (Bis-GMA) are two photocurable monomers that are extensively used in dental composites. Their toxicity is acceptably low and their mechanical strength is in an appropriate range for pharmaceutical coating (Pereira et al., 2005). The current work investigates the feasibility of using visible instead of ultraviolet light, and photocurable monomers, photoinitiators and photo-sensitizers which are generally used in dental practice (Atai et al., 2004; Hussain Latiff et al., 2005; Imazato et al., 2001, 1999; Kim and Jang, 1996; Lu et al., 2004; Mendes et al., 2005; Tarumi et al., 1999) for solventless coating.

2. Materials and methods

2.1. Materials

Two photocurable monomers, tetraethyleneglycol dimethacrylate (TEGDMA) and bisphenol A-glycidyl methacrylate (Bis-GMA), were obtained from Rohm America (Piscataway, NJ) and ESS Tech (Essington, PA), respectively. Camphorquinone (CQ), a photosensitizer, and 2-(dimethylamino) ethyl methacrylate (DMAEMA), a photoinitiator, were obtained from Aldrich (St Louis, MO). Non-pareil beads (14–18 mesh) containing FD&C#1 as a marker dye were available from Ozone Confectioners (Elmwood Park, NJ). Explotab® (sodium starch glycolate) was obtained from Penwest Pharmaceutical Co. (Patterson, NY). Lactose (spray dried, grade# 315) was available from Foremost (Baraboo, WI). Polyethylene glycol 8000 (PEG) was obtained from Dow Chemical Company (Midland, MI). Talc and sodium chloride were obtained from Fisher Scientific (Fairlawn, NJ). Ac-Di-Sol® (croscarmellose sodium) was obtained from FMC Biopolymer (Newark, DE). All materials were stored as advised by the providers.

2.2. Methods

2.2.1. Uncured material

2.2.1.1. Wetting of solid pore-forming agents by liquid monomer. The contact angles of the monomer and/or solution (TEGDMA alone and TEGDMA:Bis-GMA 50:50) on each of several pore-forming agents (lactose, Explotab®, Ac-Di-Sol®, PEG, and sodium chloride) and pellets (non-pareil beads) and talc were determined. Compacts of the powders with 10% porosity were prepared using a Carver press (Hydraulic Press, Hydraulic Unit Model # 3912, Carver Inc., Wabach, IN). The porosity of the tablet was calculated from the tablet weight, tablet volume, and thickness and true density of powders. The porosity was controlled at 10% as it was achievable for all the powder compacts. A single drop of liquid monomer was carefully placed on the compact and the contact angle between a drop of liquid monomer and each compact was determined using a magnifier and a goniometer. All experiments were performed in 10 replicates.

The drop penetration method (Hapgood et al., 2002) was also used to evaluate wetting of pore-formers by the liquid monomers. Loosely packed beds of powders (45–150 μm) were leveled in an 85 mm diameter by 18 mm deep Petri dish using a metal spatula. A syringe with a 27.5 gauge needle positioned just above the bed surface delivered a drop of liquid monomer. The time required for the drop to penetrate completely into the porous substrate was recorded. All experiments were performed in 10 replicates.

2.2.1.2. Viscosities of photocurable monomers. Viscosities of TEGDMA and mixtures of TEGDMA:Bis-GMA (100:0, 80:20, 70:30, 60:40, 50:50 and 40:60 (w/w)) were determined at room temperature by cone-plate viscometry at a shear rate of $3\,s^{-1}$ (Model# DV-I, Brookfield Engineering Laboratories, Inc., Stoughton, MA). All experiments were performed in triplicate.

2.2.2. Free films

2.2.2.1. Initiators. FTIR was used to determine the degree of conversion (i.e., crosslinking) of the coating monomer, TEGDMA, using combinations of two photoinitiators, CQ (0.5–3%, w/v) and DMAEMA (1.5–15%, w/v) using visible light at ~400 nm. The intensity of the light source (Right Touch, Work light, Model # RT-83992, Fountain Valley, CA) was measured using a light meter (Traceable® dual-display light meter, Friendswood, TX). TEGDMA and each proportion of photoinitiator–photosensitizer mixture were mixed well in the dark for 30 min to obtain a clear solution. Films composed of TEGDMA and various combinations of CQ and DMAEMA were cast separately as free films on disposable polyethylene FTIR cards (Model #0020-300, Thermo Electron, Madison, WI) by spreading a drop (5 μl) of the liquid on the card slot. Free films were made without the pore-forming agents due to the difficulty of evenly spreading films with the powdered pore-formers. The film-coated card was placed in a quartz chamber, purged with nitrogen for 3 min, and exposed to a known intensity (82500 lux) of visible light for different exposure times (30–600 s).

The degree of curing (i.e., percent conversion of monomer to polymer) was assessed by measuring the loss of the C=C peak ($1635\,cm^{-1}$) of the acrylate moiety on the TEGDMA using FTIR. The peak height at $1635\,cm^{-1}$ before and after curing provided direct measurement of the extent of curing of the monomer by the equation below. Measurements were made in triplicate.

$$\%\,\text{conversion} = \left(1 - \frac{\text{peak height at } 1635\,cm^{-1} \text{ after curing}}{\text{peak height at } 1635\,cm^{-1} \text{ before curing}}\right) \times 100$$

2.2.2.2. Film hardness. The hardness of the films was measured using the Standard Test Method for Film Hardness by Pencil Test (ASTM 3363-00). TEGDMA and Bis-GMA were mixed in several proportions (TEGDMA:Bis-GMA 100:0, 90;10, 80:20, 70:30, 60:40, 50:50 and 40:60 (w/w)). The photosensitizer and photoinitiator, CQ and DMAEMA, at concentrations of 2 and 8 wt% (totaling 10 wt% of the coating solution), respectively, were mixed into the solution of the monomers to prepare the coating liquid. The coating liquid (500 μl) was poured into a glass ring (40 mm diameter) on a glass surface in a quartz chamber, purged with nitrogen for 3 min and exposed to visible light (82500 lux) for 5 min to form a solid film. Pencils (Berol Turquoise) of increasing hardness (6B, 5B, 4B, 3B, 2B, B, HB, F, H, 2H, 3H, 4H, 5H, 6H) were held at a 45° angle and pushed along the photocured film until a pencil was found that did not scratch the film. The hardness number of the last pencil that did not scratch the film was recorded as the scratch hardness.