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Incorporation of the chemotherapy medication cisplatin into polyamide membrane

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ABSTRACT

The search for more efficient and less aggressive cancer treatment methods has intensified over the last decades and has involved many scientific areas. To provide skin cancer patients with better quality of life, this work aims to incorporate chemotherapy into polyamide membranes, functionalized by the sol–gel methodology, for controlled drug release at the target tissue. A 200-micrometer-thick flexible polyamide membrane prepared by Additive Manufacture was activated and functionalized with the alkoxide 3-chloropropyltriethoxysilane, which was followed by incorporation of the antitumor agent cisplatin. Membrane functionalization with the alkoxide was attested by infrared absorption spectroscopy, which evidenced a band at 1100 cm^{-1}, due to Si-O-Si vibration, and typical cisplatin bands at 3200 and 1600 cm^{-1}. The thermogravimetric curve revealed increased silicon oxide and platinum residues. Drug release was tested in simulated body fluid. Cytotoxicity was evaluated by the Cell Proliferation Kit, which gave IC_{50} of 23.95 μgM.

1. Introduction

Additive Manufacturing (AM) has improved. It has attracted the attention of numerous researchers especially because it affords pieces of various shapes, sizes, and complexities, with several applications [1–7]. Within AM, the Laser Sintering technique (SLS) stands out because it uses polyamide (PA) as raw material, which is excellent for bioapplications due to its biocompatibility, good mechanical properties, low cost, and easy handling [8–10] PA consists of polyethylene $(CH_2)_n$ segments separated by amide monomers (NH-CO). These peptide units allow the polymeric chains to form hydrogen bonds with other compounds.

The sol–gel process is used to prepare highly pure, homogeneous materials at mild temperatures [11–14]. The process encompasses hydrolysis and condensation reactions of the precursor alkoxide groups, to form silanol groups (−Si−OH) that can interact with other materials and substances by hydrogen bonding. In studies involving calcium salts, polymer surface modification with silanol groups has provided the polymer with bioactivity and flexibility [15–17]. Surface modification of PA pieces obtained by AM alters the physical and chemical properties of PA, leading to applications in which the modified material functions as an anticorrosive layer or as a biomaterial. Modified PA can also be endowed with temperature resistance [1,8,18,19].

PA membrane obtained by AM can be functionalized by the sol–gel methodology and incorporated with light-emitting compounds and may have potential application in skin cancer treatment [20]. Here, we have incorporated a PA membrane functionalized via the sol–gel methodology with the chemotherapy medication cisplatin for use in controlled drug release during skin cancer treatment.

2. Experimental

2.1. Polyamide (PA) membrane preparation, washing, and activation

PA membrane obtained by AM at the Tridimensional Technology Division of the Information Technology Center Renato Archer was used. First, the PA membrane was washed with 30.0 mL of distilled water, under stirring, to remove the PA powder that had not been sintered. Next, the PA membrane, which measured 8.0 × 5.0 cm and had thickness of 200 μm, was cut into 1.0-cm^2 units with approximate mass of 25.30 mg and dried. Then, the PA membrane was pretreated as described in [21]. Briefly, the PA membrane was immersed in 1.0 mol L^{-1} acetic acid under stirring for 24 h, washed with distilled water in ultrasound bath, and dried at ambient temperature for 24 h. This treatment activated the membrane surface by protonating the PA amide groups.

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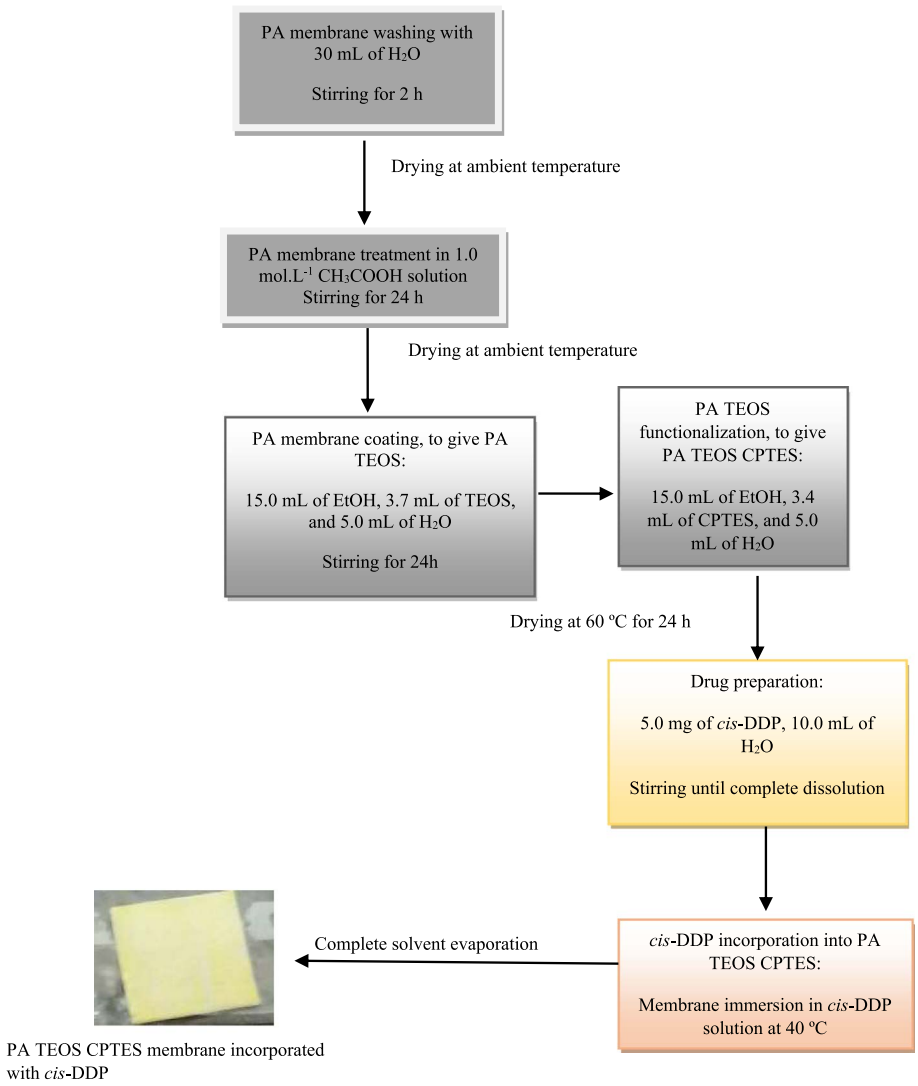
Fig. 1. (a) Functionalized polyamide membrane (PA TEOS CPTES) obtained via the sol–gel methodology; (b) PA TEOS CPTES after cisplatin (*cis*-DDP) incorporation.



Flowchart 1. Representation of functionalized polyamide membrane (PA TEOS CPTES) preparation and incorporation with the chemotherapy medication cisplatin (*cis*-DDP).

2.2. PA membrane functionalization with the alkoxides tetraethyl orthosilicate (TEOS) and 3-chloropropyltriethoxysilane (CPTES)

The 1.0-cm^2 PA membrane was placed in a two-neck round-bottom flask containing 15.0 mL of ethanol (EtOH), 3.7 mL of TEOS, and 5.0 mL of distilled water. The mixture was kept under reflux and constant stirring at 80 °C for 24 h. After this process, the membrane was washed with distilled water in an ultrasound bath and dried at 60 °C for 2 h. The resulting sample, designated PA TEOS, was functionalized with 3.4 mL of the alkoxide CPTES in the same conditions described above, to give the sample labeled as PA TEOS CPTES [20].

2.3. Cisplatin (cis-DDP) incorporation into PA TEOS CPTES

The *cis*-DDP solution was prepared by dissolving 5.0 mg ($1.66.10^{-2}$ mols) of *cis*-DDP in 10.0 mL of distilled water under constant stirring for 20 min.

Drug incorporation into PA TEOS CPTES was accomplished by the casting method. PA TEOS CPTES was placed in a *cis*-DDP solution at 40 °C until the solvent evaporated completely. PA TEOS CPTES became