



Electrochemically driven reagent release from an electronic suture



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ABSTRACT

Sutures loaded with growth factors or antimicrobials are commonplace but the release of the therapeutic agent is almost invariably achieved through passive release mechanisms. A gold microwire loaded with cellulose acetate phthalate encapsulated drug droplets is proposed as an alternative design approach. The release mechanism relies upon the imposition of a suitable reducing potential at the gold suture resulting in an increase in local pH and thereby induces the dissolution of the polymeric binder and releases the drug. The ability to actively control the dissolution-release processes could lay the foundations for smart suture design where more responsive/metered dosing could be achieved.

1. Introduction

Sutures are an invaluable tool in the treatment of major wounds, where they offer a speedy method of binding apposing tissues and, in principle, can facilitate wound healing [1–4]. While the general mechanism of wound closure has changed relatively little in recent years, the materials employed in the manufacture of sutures have evolved considerably. Biodegradability, physical structure and chemical composition are the key factors subject to manipulation and there is a wealth of commercially available variants [2,3]. Sutures possessing antimicrobial activity are now commonplace and have arisen partly in response to the long-standing issues of surgical site infection (SSI) [3]. The latter are generally acknowledged as being the most commonly incurred postoperative complication and represent 15–20% of all nosocomial infections arising after surgery [5,6]. It has been demonstrated that sutures loaded with antimicrobial agents (such as triclosan or silver nanoparticles) reduce infection rates and improve wound recovery [2,3,6–10]. Irrespective of design, commercial sutures are typically based on a thread-like form to provide the mechanical resilience needed to draw the wound edges together and, thereafter, the antimicrobial features are invariably delivered through passive interaction with the surrounding tissue [2]. Given the increasing concerns over antimicrobial resistance, there is a need for further improvements in suture design where the latter is capable of providing a more active role – either through providing diagnostic telemetry of the healing dynamics or enabling the targeted delivery of drugs to the site of infection. The aim of the present communication is to evaluate the use of a gold–silver composite thread as a platform through which electronic sutures capable of controlling the release of a chemical agent could be developed.

Kim and colleagues (2012) demonstrated a microfabricated strip sensor capable of sensory feedback and actuation and have heralded a step change in suture design [11]. The present investigation has similarly sought to explore controlled actuation through a potentially simpler, though more versatile and easily implemented electrochemical route. The rationale revolves around the encapsulation of the model drug (Toluidine Blue O, TBO) within cellulose acetate phthalate (CAP) droplets which are dispersed along the length of a gold microwire (25–100 μm diameter) as indicated in Fig. 1. The CAP polymer binder is pH sensitive and is extensively used in oral tablet formulations to enable delivery of drug to the intestine where the alkaline environment dissolves the protective coating [11–16]. Thus, it was envisaged that upon the imposition of a suitably reducing potential (-1 V to -2 V) at the gold electrode, the local pH will increase and the CAP droplets should dissolve and thereby release the drug [17].

The wire itself lacks the necessary tensile strength to pull the wound surfaces together but can be incorporated as an additional component within a conventional suture thread. A commercial silver thread is employed as both the structural suture backbone and second electrode in the electrochemical design. This report examines the electrochemical behaviour of the various components and assesses the efficacy of the proposed mechanism.

2. Experimental details

Electrochemical measurements were conducted using a $\mu\text{Autolab}$ computer controlled potentiostat (Eco-Chemie, Utrecht, The Netherlands). All measurements were conducted at $22\text{ }^\circ\text{C} \pm 2\text{ }^\circ\text{C}$ in Britton Robinson buffer (pH 3–10) unless stated otherwise. Gold and

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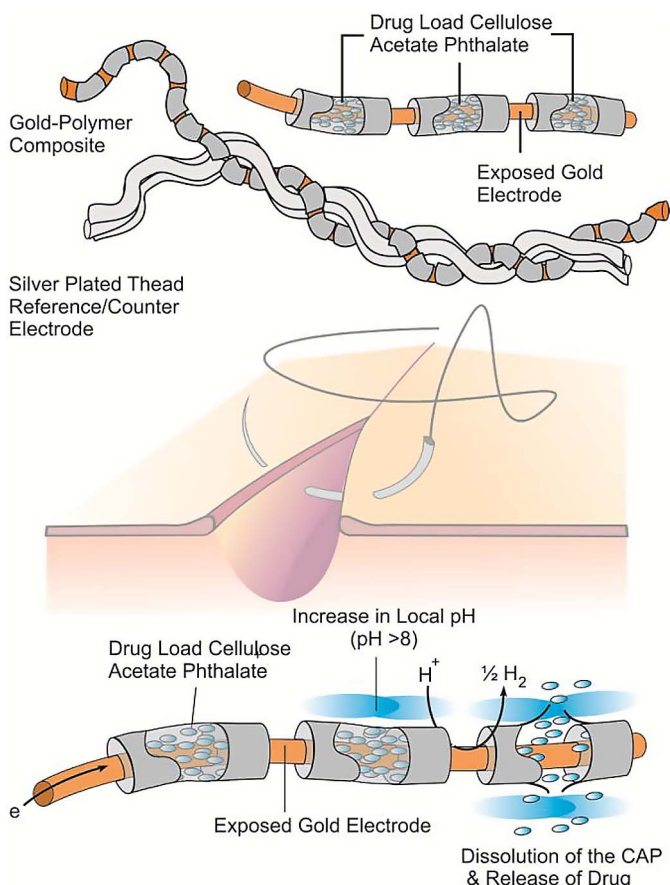


Fig. 1. Proposed controlled release methodology.

silver wires were supplied by Goodfellow Ltd. In cases where a three-electrode configuration was employed, a silver/silver chloride half cell (3 M NaCl, BAS Technicol) served as the reference. Conductive silver thread (0.4 Ω /cm) was supplied by Kitronik Ltd. (Nottingham UK). The thread is composed of 96 individual filaments, each coated with a micron-thick layer of silver. The fabrication process involves a primary twist comprising 16 filaments of cotton. Two primary twists are subsequently wound together to form the secondary twist and finally three of the latter are combined to yield the final thread consisting of 96 filaments and is approximately 18 denier. The Toluidine Blue O (5 wt%) was mixed with the CAP polymer through dissolution in acetonitrile and then dropped and spread along the length of the gold wire. While it was initially anticipated that application of the TBO/CAP mixture to the gold would have led to a coherent film, the polymer spontaneously coalesced into discrete droplets along the length of the wire as a consequence of poor surface wetting. This coating process was repeated up to 4 times to increase the yield of TBO. Electrochemical release was induced through holding the potential at -1 , -1.5 , -1.75 or -2 V for a given period (typically 10 s) and then recording the absorbance spectrum (200–800 nm) in a 1 cm³ volume cuvette.

3. Results and discussion

The efficacy of employing cellulose acetate phthalate as the controlled release polymer was briefly assessed using gelatin as the simulated tissue matrix. Toluidine Blue O was used as a model drug as its release could be readily monitored through visual inspection ($\lambda_{\text{max}} = 591$ nm, $\epsilon = 2.98 \times 10^3$ L⁻¹ mol⁻¹ cm⁻¹) or, as detailed later, through UV-vis spectroscopy. The thread was initially washed to remove interfacial TBO such that only the dye encapsulated within the polymer matrix remained. The thread was then immersed in gelatin samples whose pH had been previously adjusted and left for up to 48 h.

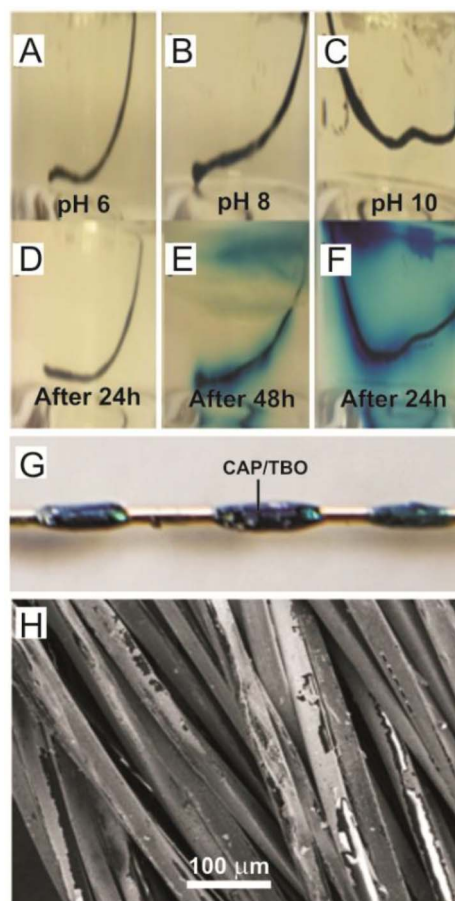


Fig. 2. Release of Toluidine Blue O from cellulose acetate polymer coating on thread immersed in gelatin of varying pH (A–F). (G) Gold microwire (100 μ m) modified with CAP/TBO droplets. (H) Electron micrograph of the silver suture thread. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

The results of the study are highlighted in Figs. 2A–F, where it can be seen that the TBO only emerges when the pH is alkaline. Dissolution of the cap was found to be extremely slow from neutral or mildly alkaline (pH 8) with diffusion of the TBO into the surrounding gelatin observed only after 48 h.

The CAP/TBO droplets positioned on the gold wire (100 μ m) are shown in Fig. 2G, though their relative positioning is exaggerated for clarity. The structure of the conductive thread is highlighted in Fig. 2H and it can be seen that, while silver coats each of the individual fibres within the braid, there are sections where the underlying cotton is exposed. This is consistent with previous reports of electroless deposition of silver on fabrics and can be expected where the plating solution has failed to nucleate on particular areas or where the braiding has prevented sufficient penetration [18–20]. Nevertheless, the silver deposition clearly extends along the length of the thread and is sufficiently coherent to retain conductivity when twisted or sewn, which is ideal for the proposed application. It should be noted that the prime rationale for the commercialisation of the thread was targeted at emerging ‘e-fabric’ and wearable electronics and designed specifically for sewn and woven applications. The ability of the thread to serve as a viable reference/counter electrode was assessed through comparing the potentiometric response to chloride ion whereby a Nernstian response (-59 mV) was obtained. The tensile strength of the conductive thread was investigated and found to be 1.6 N/Tex (%RSD = 9.1; $N = 6$) which compared well with a conventional Vicryl® braided suture (0.57 N/Tex) [21]. Thus it could be expected that the electronic thread would provide the necessary strength to draw the apposing wound surfaces together and enable

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