Electro-responsive drug delivery systems based on 3D graphene-based double-network

H.C. Bidsorkhi[1,2], N. Faramarzi[1,2], L. Di Muzio[3], A.G. D'Aloia[1,2], M.S. Sarto[1,2]

[1] Dept. of Astronautical, Electrical and Energy Engineering (DIAEE), Sapienza University of Rome, Italy

[2] Research Center for Nanotechnology Applied to Engineering (CNIS), Rome, Italy

[3] Dept. of Drug Chemistry and Technologies, Sapienza University of Rome, Italy

In the context of personalized medicine, wearable drug delivery devices capable of programmable and non-invasive therapeutic release are urgently needed. This work presents a next-generation, wearable electro-responsive platform for controlled and on-demand transdermal drug delivery. The system integrates a novel double-network hydrogel composed of poly(vinylidene fluoride) (PVDF)–graphene nanoplatelet (GNP) aerogels and calcium-crosslinked sodium alginate, designed to respond to low-voltage electrical stimulation.

The engineered composite addresses the limitations of traditional transdermal systems, such as limited control over release kinetics and poor mechanical robustness, by combining the electrical conductivity and mechanical stability of PVDF-GNP aerogels with the hydrophilic, drug-loading capabilities of alginate hydrogels. The unique synergy between these components creates a flexible, biocompatible matrix that allows precise, user-triggered modulation of drug release without thermal side effects.

The device comprises a PVDF-GNP aerogel prepared via thermal exfoliation of graphite and solvent processing, followed by formation of a double network through diffusion of 3% w/v sodium alginate and ionic crosslinking with 3% w/v $CaCl_2$. A model drug, theophylline, was incorporated into the alginate phase to study entrapment and release efficiency. Electrical stimulation protocols were applied via embedded gold electrodes in a Franz cell setup, with release monitored using HPLC.

SEM analyses confirm a highly porous and homogeneously structured aerogel scaffold. The inclusion of 11 wt% GNPs enhances both electrical conductivity and mechanical performance. The double-network formation is validated through release studies, showing improved drug retention compared to non-crosslinked systems.

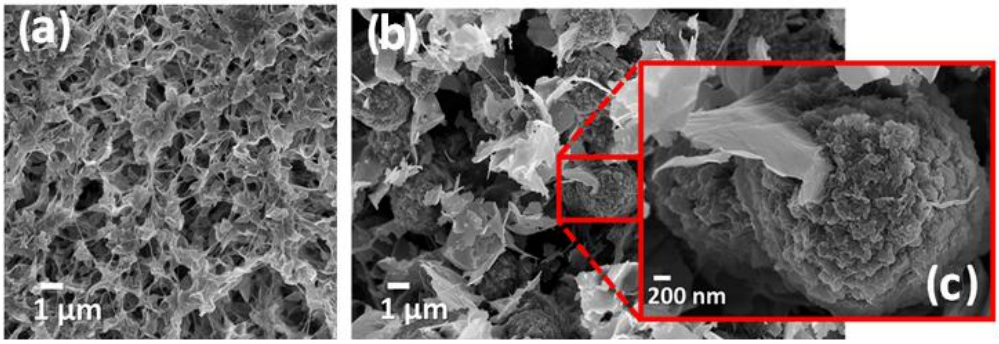

Figure 1. SEM images of produced samples of neat PVDF aerogel (a) and of GNP-PVDF aerogel (b).

The drug entrapment efficiency reached values exceeding 60%, a significant improvement attributed to the high surface area and interconnectivity of the aerogel network. Electrical pulses (e.g., 1V for 30s every 5 min over 1 h) elicited a steady release profile, reaching ~3% of total drug

content with minimal heating (T ≤ 35°C). More aggressive protocols (3V for 10s, 6V for 10s, or higher frequency) resulted in higher and faster drug release rates.

To further evaluate tunability, Fig. A and B show comparative release profiles under different stimulation protocols. As shown in Fig. A, applying pulses of 6V for 10 seconds every 3 minutes resulted in the highest release (over 12%), followed by lower-voltage or shorter-duration protocols. Fig. B shows an overall lower release profile for a different batch or loading condition, though the trends remain consistent: increased voltage and frequency correlate with higher cumulative release. The stepwise release pattern reflects the system's responsiveness to each stimulation pulse. Importantly, temperature remained stable during all tests, confirming the safety of the electro-actuation approach.

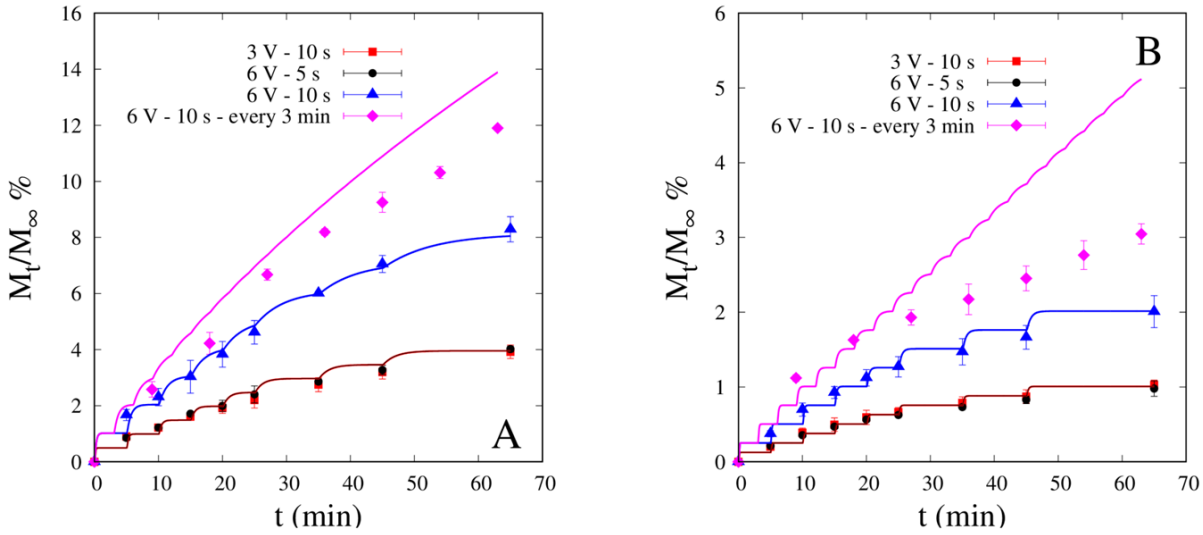

Figure 2. A and B show comparative release profiles under different stimulation protocols.

Unlike existing iontophoretic patches or hydrogel systems, our device enables direct electrical actuation of drug release from within the matrix, eliminating the need for external drug reservoirs. Its mechanical stability, reusability, and responsiveness at low voltage make it ideal for wearable formats.

In conclusions, we report the development of a wearable, on-demand drug delivery system leveraging the synergy of PVDF-GNP aerogels and alginate hydrogels in a double-network configuration. This device offers significant advances in personalized therapeutics, with potential applications in chronic pain management, hormone therapies, and other fields requiring precision dosing. Future work includes in vivo biocompatibility testing, integration with wireless control units, and exploration of multilayer formulations for multi-drug release.

This research has been financed by "WAYBACK- Wearable SmArt Devices for communitY-based low BACK pain rehabilitation", PRIN– Bando 2022, Prot. 2022HNBRKL.

References

1. H.C. Bidsorkhi, L. Di Muzio, A.G. D'Aloia, P. Paolicelli, M.A. Casadei, M.S. Sarto, "D Porous Graphene-Based Double Polymeric Networks for Controlled Drug Delivery" Graphene 2019 – June 25-28 (Rome, Italy).