Virus titration and paper-based device to assess the effectiveness of stimuli-responsive copper-modified mesoporous silica nanoparticles as a smart antimicrobial delivery system for SARS-CoV-2

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Introduction

The worldwide outbreak of the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) in 2020 has led to an unprecedented global health crisis, with a deep impact on healthcare and economic systems of modern societies. In this context, timely and rapid diagnostic approaches capable of detecting viral antigens, as well as preventing uncontrolled viral release through functionalized surfaces with antimicrobial delivery properties, are essential for the most effective response to an infectious disease outbreak [1, 2].

Herein, copper-modified mesoporous silica nanoparticles (Cu-MSNs) have been functionalized with Poly(2-(diethylamino) ethyl methacrylate) (PDMAEMA) brushes and loaded with carvacrol. To assess the pH-responsive effect, the study was carried out at different pH levels, and the release of carvacrol was demonstrated using a paper-based electrochemical device [3], customised for this application.

Both copper and carvacrol, employed for the functionalization of MSNs, exhibit strong inhibitory activity against several viruses through distinct mechanisms. In particular, copper ion binding, cross-linking between genome strands and the copper toxicity generated by ROS result in damage to the genome [4]. In addition, carvacrol influences the virus's ability to enter host cells by targeting viral membranes and the virion capsid [5]. In this context, the virucidal effectiveness of Cu-MSNs-Poly DMAEMA with and without carvacrol was evaluated against SARS-CoV-2.

Aim

1. Investigate the pH – dependent release of the essential oil in Cu-MSNs Poly DMAEMA loaded with carvacrol by a paper-based electrochemical device;

2. The evaluation of the virucidal activity of the Cu-MSNs-Poly DMAEMA-carvacrol against SARS-CoV-2

Methods

Figure 1. Study of Cu-MSN- PDMAEMA particles smart-leaching of carvacrol using an electrochemical paper-based sensor

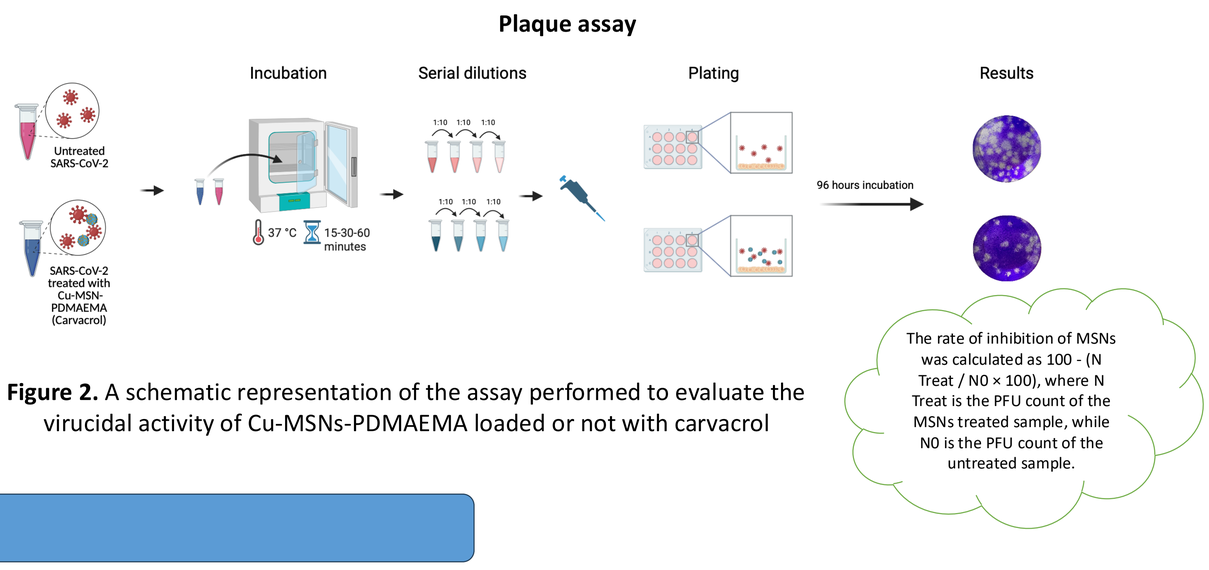

Figure 2. A schematic representation of the assay performed to evaluate the virucidal activity of Cu-MSNs-PDMAEMA loaded or not with carvacrol

Results

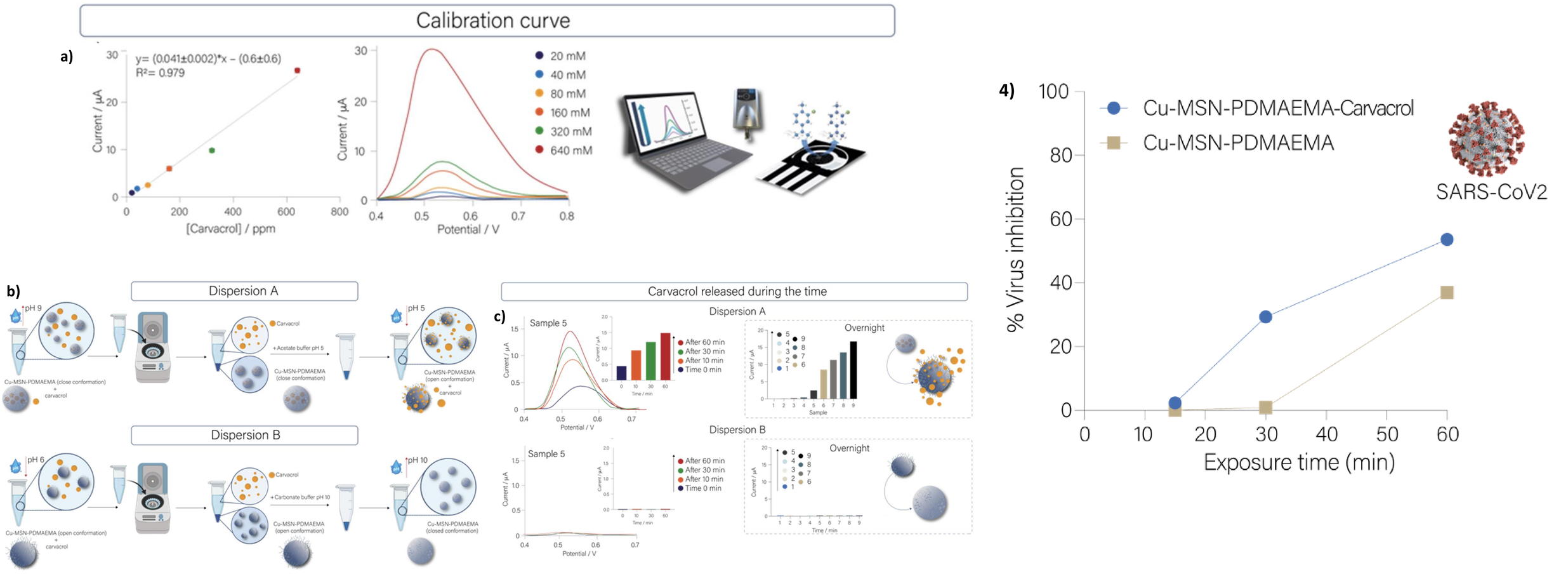

Figure 3. Study of Cu-MSN-PDMAEMA particles smart leaching of carvacrol using an electrochemical paper-based sensor. a) Calibration curve of EOs using the paper-based electrochemical sensor. b) Schematic illustration of preparation of dispersion A and B. c) Study of carvacrol release over time by using dispersion A and dispersion B.

Figure 4. Virucidal activity of Cu-MSNs-PDMAEMA and Cu-MSNs-PDMAEMA Carvacrol. SARS-CoV-2 inhibition (%) with Cu-MSN-PDMAEMA-carvacrol and Cu-MSN-PDMAEMA as a function of exposure time (15-30 and 60 minutes).

Conclusions

The paper-based electrochemical sensor used to evaluate carvacrol loading and release demonstrated the pH-responsive behaviour of the Cu-MSN-poly DMADEMA nanoparticles. In fact, the results indicated the smart release of carvacrol from Cu-MSN-PDEAEMA under low-pH conditions (pH<6) and, conversely, the ability to trap the essential oil when maintained at pH>9. These findings highlight the potential of these particles as an antibiotic-free alternative for preventing microbial infections while mitigating the development of AMR.

When tested against the enveloped virus SARS-CoV-2, Cu-MSN-PDMAEMA showed virucidal activity below 50% at the highest time point tested (60 minutes). A comparison of Cu-MSN-PDMAEMA functionalised with carvacrol showed a trend towards higher virucidal activity than Cu-MSN-PDMAEMA, although the differences were not statistically significant ($p>0.05$, Welch test). By contrast, the virucidal effects of carvacrol-Cu-MSN-PDMAEMA increased gradually over time, with a trend from no virucidal activity after 15 minutes to the maximum value after 60 minutes, and this increase was statistically significant.

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