

TaffiX® Nasal Powder forms an Effective Barrier against SARS-CoV-2

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ABSTRACT

TaffiX® is a personal, anti-viral nasal powder that is commercially available in Israel and Europe. To test if

TaffiX® was able to form a protective barrier against SARS-CoV-2 gels of TaffiX® were formed on nylon filters, and then seeded with SARS-CoV-2. After 10 minutes the bottom of each filter was washed and tested for live virus by plaque assay and viral RNA using qRT-PCR. TaffiX® blocked SARS-CoV-2 in vitro, reducing the titer of live virus and viral RNA by 99%, supporting the use TaffiX® as a barrier against SARS-CoV-2 that could be used in conjunction with other protective measures.

Keywords: Infectious Diseases; Viral Fever; Quantitative Research

Introduction

Effective measures that reduce exposure to the SARS-CoV-2 virus are an important aspect of containing the COVID-19 pandemic. In the absence of a protective vaccine and with growing evidence that presymptomatic and asymptomatic transmission of SARS-CoV-2 are significant factors contributing to spread of infections [1],

there is a need for mechanisms that can reduce exposure to the virus. The cellular entry of SARS-COV-2 depends on the binding of the spike (S) protein to a specific cellular receptor, angiotensin-converting enzyme [2] (ACE2), and subsequent S protein processing by cellular proteases. ACE2 and other proteases are highly expressed in ciliated and goblet nasal cells, which supports the growing understanding that nasal infection is the dominant route of transfection for COVID-19 viruses and therefore protection of the nasal epithelium is an effective means of controlling infection [3,4].

Hou et al. describe the “infection gradient” whereby SARS-CoV-2 shows a gradient infectivity from the proximal to distal respiratory tract, with ciliated airway cells and AT-2 cells as primary targets for SARS-CoV-2 infection [5]. The authors conclude that the nasal epithelium is an important gateway and therefore its protection could dramatically decrease the risk of viral infection

and transmission. TaffiX®, a nasal hydroxypropyl methylcellulose (HPMC) based powder spray, is a semisynthetic, inert, viscoelastic muco-adhesive polymer used frequently in the pharmaceutical industry. HPMC is used in eye drops, as an excipient and controlled-delivery component in oral medications, and found in a variety of commercial products including several nasal powder products used as prevention of allergy [6,7]. Polymer-based powder formulations show no adhesion until their absorption of mucus occurs on the nasal mucosa surface. This allows easy application to the nasal cavity by nasal insufflation even if the polymer is highly mucoadhesive [8].

TaffiX® creates an acidic gel (pH 3.5) once it has reached the nasal mucosa thus creating a local hostile microenvironment to viruses at a pH range known to be associated with viral death [9]. TaffiX® also contains benzalkonium chloride which is known as an antimicrobial preservative and was shown by Chin et al. to inactivate SARS-COV-2 [10]. This study we report that TaffiX® was able to form a protective barrier against SARS-CoV-2 virus using experimental in vitro conditions that reduced the titer of recoverable live virus as well as viral RNA by 99%.

Materials and Methods

Taffix® Assay

One hundred-fifty ml of sterile water was added to individual sterile 40 mm cell strainers (BiologGLX) in the wells of a 6 well plate. Twenty mg Taffix® was added and mixed with the water with a pipet tip until homogeneous across the cell strainer surface, and incubated at room temperature for 10 min. Control filters were incubated with 150 ml of sterile water. Ten ml virus was added to the center of each cell strainer and incubated at room temperature for another 10 minutes. The bottoms of the cell strainers were washed with 500 ml serum-free DMEM and flow through was collected for RNA isolation and plaque assays.

Plaque Assay

Plaque assays were performed as described in [11]. Vero C1008, Clone E6 (ATCC CRL-1586) cells were grown in DMEM (GIBCO 11995-040) and then seeded into [12]-well tissue culture plates at a concentration of 2×10^5 cells/well the night before the assay. Viral stocks were diluted in cold serum free DMEM and added to the wells. Plates were incubated at 37°C, 5% CO₂ for 2 hours, and swirled every 15 min. After two hours the media was replaced with 1.5 ml of 1X DMEM, 2.5% FBS, 1.2 % Avicel PH-101 (Sigma Aldrich) and incubated at 37°C, 5% CO₂. After two days the Avicel was removed and the wells were washed with 1 ml of PBS. Ten percent formaldehyde was added. After 1 hr wells were washed with PBS, and then 0.1% crystal violet was added for 30 minutes and then washed with water.

Quantitative Reverse Transcriptase PCR (qRT-PCR)

RNA was isolated from 200 ml of the flow through wash from the Taffix® assay using QIAamp Viral RNA Mini Kit (Qiagen) according to manufacturer's instructions. The PCR reaction consisted of

UltraPlex 1-Step ToughMix (Quantabio) and a combined primer/probe mix 2019-nCov_RUO kit (Integrated DNA Technologies). The positive control was 2019-nCov_N Positive Control. The reaction conditions were 50°C for 10 min, 95°C for 3 min, and then 45 cycles of 95°C for 20 sec, 55°C for 30 sec.

Taffix® Gel formation in Pig Noses

The Taffix® powder (4 puffs per nostril, parallel to 1 puff per human nostril as indicated in product instructions) was sprayed on a fresh slices of pig nasal cavity, obtained from a meat processing plant, which was then soaked in saline and then placed in an oven at 34°C to resemble the human nose conditions and clinical dose per surface area. A blue color (Instacoat Color Blue, Ideal Cures Pvt. Ltd.) was mixed with powder before spraying for visualization. The gel formation time, and appearance were noted. The pH was measured with pH-FIX sticks (range 3-6, Macherey-Nagel) for 5 hours.

Results

To test whether the Taffix® can form a protective barrier against SARS-CoV-2, a gel of Taffix® was formed on a 40 mm nylon filter using an amount equivalent to a clinical dose of 5 mg per nostril, the recommended usage dose. 10,000 PFUs of SARS-CoV-2 was applied to the Taffix® gel-treated filter; the same amount of virus was added to an untreated filter as a control. After a 10 minute incubation, the bottom of each filter was washed and the resulting flow through tested for live virus by plaque assay and viral RNA using qRT-PCR. Taffix® reduced the amount of infectious virus in the flow through by more than 99% (Figure 1A), with an average three log reduction in titer. The number of copies of the viral genome recovered was also decreased by 99% by Taffix® treatment as determined by qRT-PCR (Figure 1B), with an average drop in copy number of over two logs, although detection of viral RNA does not necessarily represent infectious virus.

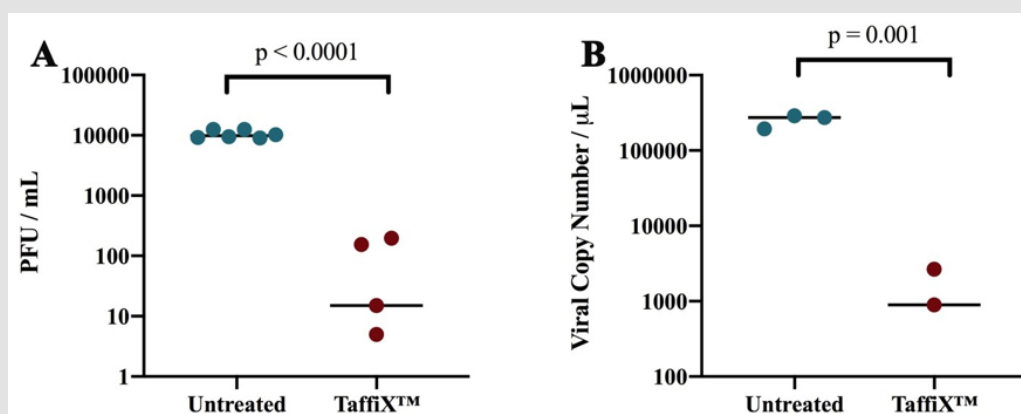


Figure 1: Taffix® treatment reduces the amount of infectious SARS-CoV-2 virus. A) Viral titers of live virus in the flow through as determined by plaque assay. B) Copies of viral RNA as determined by qRT-PCR in Taffix®-treated and untreated SARS-CoV-2 flow through. P values were determined by two tailed Student's T test. Data represents 6 (plaque assays) and 3 (qRT-PCR) biologically independent experiments. One Taffix treated sample in panels A and B had no detectable virus or viral RNA so they are not represented.

To test the stability of the gel pH on nasal tissue *ex vivo*, the powder was sprayed on a fresh slices of pig nasal cavity soaked in saline solution and placed covered in an oven at 34°C to resemble the human nose conditions and clinical dose per surface area. The gel formation time, and gel appearance during 6 hours were monitored as well as gel pH. TaffiX® powder formed a uniform gel on a pig nasal cavity tissue within 1 minute from spray and was stable as a gel film for 6 hours. The initial pH of the gel was 3.6 and the final (after 6 hours) pH 109 was 4.4.

Discussion

Under *in vitro* conditions, TaffiX® formed a protective barrier against SARS-COV-2. Although these are artificial conditions, *ex vivo* experiments with pig nasal tissue demonstrated that a TaffiX® gel is formed within 1 minute from spray and an acidic film is maintained on the tissue for at least 5 hours. Without the gel protection, the human nasal mucosal pH is approximately 5.5-6.5 [12], which is a comfortable environment to SARS-COV-2 virus. Clinical study by Hull et al. demonstrated in a randomized, double blind, placebo- controlled study that irrigation with an acidic nasal hydrogel spray reduced the severity and duration of the common cold symptoms [13]. TaffiX® is a safe and easy to use powder that may provide a straightforward mechanism to reduce infections and thus the spread of COVID-19.

Declaration of Competing Interest

T. Lapidot, PhD and D. Megiddo, MD are employees of Nasus Pharma.

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Footnote

TaffiX® is approved in Israel (Amar: 33010001) with the following Indication for Use: TaffiX® is intended for use to block inhaled viruses and bacteria within the nasal cavity. TaffiX® is legally marketed in Europe (CE- DE/CA09/0760/N18/001) with

the following Indication for Use: TaffiX® is indicated for use as a protective mechanical barrier against allergens and viruses (e.g., SARS-CoV-2) within the nasal cavity.

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