Taffix- mechanism of action

Dalia Megiddo, MD, MBA, CEO, Nasus Pharma

Contents

1 PRODUCT DESCRIPTION AND MECHANISM OF ACTION:

Nasus Pharma developed Taffix™ - an innovative nasal powder inhaler that is able to effectively block viruses from reaching nasal mucosa. The nose is the main gateway of airborne droplet viral infection to the body. As such Taffix™ will add a significant protective tool for *preventing viral infections* in addition to the multiple preventive measures taken today.

Figure 1: Taffix

Nasus Pharma's unique compositions and manufacturing technology generates uniform microspheres of pharmaceutical materials such as API and excipients. Based on this technology Nasus developed HPMC based nasal powder – Taffix™- that creates a thin uniform gel over the nasal mucosa and mechanically prevents viruses from reaching the nasal epithelium.

More important-

Taffix™ creates a local microenvironment pH of 3.5 – a pH known to be associated with up to 99.99% of viral death. Nasus tested its products in several in vitro studies that proved its efficacy in blocking viruses from reaching and infecting human cells.Taffix was also tested in a real-life high infection risk setting and reduced the risk of infection by 78%.

It is important to remember that Taffix™ should be used in addition to ALL safety measured such as masks gloves and social distancing adding a layer of protection.

Nasus Pharma received CE marketing approval (DE/CA09/0760/N18/001) and the Israeli Ministry of Health marketing authorization (Amar- 33010001) and is currently commercially available in Israel Europe and South America.

2 THE NOSE IS THE MAIN ENTRY GATE FOR SARS -COV-2 INFECTION

Coronavirus disease 2019 (COVID-19) is a respiratory illness that results from infection in Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2).[1] Cases have been detected in most countries worldwide and community spread is being detected in a growing number of countries. On March 11, the COVID-19 outbreak was characterized as a pandemic by the WHO.

Early reports suggested that person-to-person transmission most commonly happens during close exposure to a person infected with COVID-19, primarily via respiratory droplets produced when the infected person coughs or sneezes. Droplets can land in the mouths, noses, or eyes of people who are nearby or possibly be inhaled into the lungs of those within proximity. [2]

Recent research that analyzed several biological specimens for detection of SARS-CoV-2 (COVID- 19), [3] concluded that nasal swabs had the highest mean cycle threshold value of 24.3 (1.4×10^6 copies/mL) of the virus, indicating higher viral loads compared to other nasopharyngeal, oral, lung, blood and other specimen.

As our knowledge of the COVID-19 grew it became clear that the cellular entry of coronaviruses depends on the binding of its spike (S) protein to a specific cellular receptor (ACE-2) and subsequent S protein priming by cellular proteases. Recently a

study by Sungnak et al[4] published in Nature Medicine described the significantly higher expression of ACE-2 and other proteases in ciliated and goblet nasal cells thus solidifying prior knowledge that the nasal epithelium is the major entrance gate of the COVID-19 into the body and most transfections occur on the nasal epithelium. Recent articles support the growing understanding that nasal infection is the dominant route of transfection for COVID-19 viruses and emphasize the dire necessity of protecting the nasal epithelium as the most effective mean of controlling the infection.[5] Hou et al describe the "infection gradient" whereby SARS-CoV-2 shows a gradient infectivity from the proximal to distal respiratory tract. Ciliated airway cells and AT-2 cells are primary targets for SARS-CoV-2 infection. The author conclude that nasal epithelium is an important gateway and its protection could therefore change dramatically the risk of viral infection and transmission.

3 RATIONALE FOR THE MECHANISM OF ACTION:

Taffix mechanism of action is based on the following proven scientific approaches:

1. It is possible to block viruses extracellularly through local effect in the nose.
2. Non specific blocking of viruses and preventing respiratory infection through the creation of low pH gel over the nasal mucosa is clinically proven as effective.
3. It is possible to lower the local pH in the nasal cavity.
4. Respiratory viruses and SARS-CoV-2 virus are sensitive to low pH

Before delving into the specific studies performed with Taffix to test and prove it's efficacy there is a need to briefly discuss these approaches and their proof in prior studies:

3.1 EXTRACELLULAR BLOCKING OF VIRUSES IN THE NOSE IS EFFECTIVE IN PREVENTING VIRAL INFECTION.

Hayden et al tested the hypothesis that it is possible to block viruses before they enter and infect nasal cells thus preventing respiratory infection in a series of preclinical and clinical studies using GG167 (later called zanamivir or Relenza). Zanamivir has no systemic effects and is only active locally over respiratory epithelium. Four randomized, double-blind, placebo-controlled clinical studies comprised a total of 166 volunteers that received nasal solution of Zanamivir as a prophylactic treatment and then were

infected with H1N1 influenza virus showed that prophylaxis was 82% effective in preventing laboratory evidence of infection and 95% effective in preventing febrile illness. The investigators conclude that It is possible to block viruses and prevent infection by using local effect in the nose [6].

3.2 CREATING NON DRUG, NON SPECIFIC INHIBITORY ENVIRONMENT (HPMC, LOW PH) IN THE NASOPHARYNX WAS FOUND CLINICALLY EFFECTIVE IN CONTROLLING VIRAL INFECTION.

Non specific extracellular blocking of viruses was described using mechanical lining of the nasal epithelium with gel forming mucoadhesive polymers. (HPMC). Hull et al[7] conducted a large multicenter randomized parallel double-blind study that included 1000 patients in 5 groups testing the efficacy of several formulations in reducing the severity of common cold. All formulations comprised of mucoadhesive polymers and buffered to a pH of 3.5. Two of the formulations were based on HPMC in different concentrations. Participants were asked to start using the nasal formulation at the first signs of cold. The study, aimed at testing the effects of creating a non-specific, virus-hostile environment in the nasopharynx on the symptoms and duration of Common Cold, demonstrated the higher efficacy of HPMC formulation in reducing disease severity. Of note: the most effective formulation was essentially almost identical to Taffix with just a different buffer used to create the low pH (citric acid and sodium citrate in Taffix vs L-pyroglutamic acid, succinic acid and disodium succinate in the formulations used in the study). None of the test formulations buffers are approved as nasal inactive ingredients whereas citric acid and sodium citrate are approved as inactive ingredient for nasal spray) .The investigators conclude that, the results of this study suggest that the creation of a non virus-specific low pH inhibitory environment in the nasopharynx holds promise as an effective method of controlling the severity and duration of naturally acquired Common Cold infections.

3.3 LOW PH CAN BE CREATED IN THE NOSE AND WHEN IT IS IN GEL IT IS MORE EFFECTIVE.

Gern and his group[8] working with Proctor and Gamble on the development of low pH nasal formulation to block and inactivate rhinoviruses conducted a series of in vitro, animal and clinical studies to measure the tolerability safety and effect of different formulations. Although not all formulations (solution based and not gel based) were

found effective- all were found safe and well tolerated when compared to saline solutions (in effect: less irritative than saline) , The results demonstrate that it is possible to lower the nasal pH to <4.0 in healthy human subjects by dosing with as little as 50–100 µL of nasal spray. Encouragingly, effects on pH in the nasal cavity extended from anterior portion of the inferior turbinate (where the product was deposited) to the nasopharynx, indicating a broad pattern of deposition and/or spread. Overall, dilution into nasal secretions and buffering in the nasal tissues resulted in a change of only 0.5 pH units from the delivered product. In a follow on article from the PG research group the investigators found that adding a mucoadhesive polymer (e.g HPMC) is more effective in prevention of viral infection both in vitro and in a ferret animal model. [9] The investigators conclude that low pH gel intranasal sprays inactivate influenza viruses in vitro and protect ferrets against influenza infection.

3.4 RESPIRATORY VIRUSES ARE SENSITIVE TO LOW PH :

A survey of the literature shows that most common respiratory viruses are sensitive to low pH:

Table 1: Common causes of respiratory viral infection [10]

Rhinoviruses	54%
Corona viruses	14%
Influenza	9%
Parainfluenza	4%
RSV	2%
Adenovirus	2%
Other viruses	2%
Bacteria or unknown	13%

Studies demonstrating the high sensitivity of all respiratory viruses to low pH are abundant in the scientific literature for several decades. The table 2 is a short summary of studies that demonstrated the different sensitivity of respiratory viruses to low pH: All viruses do not survive at pH levels of 3.5.

Table 2: Respiratory viruses' sensitivity of low pH

Virus	Loss of infectivity pH	Reference
Rhinovirus – 26 different strains	4	Johnston SL: Anti-influenza therapies. Virus Research 2002, 82:147–152.
Rhinovirus type 14	3 and 5	Hughes JH, Thomas DC, Hamparian VV: Acid lability of rhinovirus type 14 : effect of pH, time and temperature. Proc Soc Exp Biol Med 1973, 144:555–560.
Influenza (three strains: Hong Kong, Influenza A Sydney/5/97and avian)	3.5	Rennie, P., Bowtell, P., Hull, D. et al. Low pH gel intranasal sprays inactivate influenza viruses in vitro and protect ferrets against influenza infection. Respir Res 8, 38 (2007). https://doi.org/10.1186/1465-9921-8-38
Rhino viruses	6.2	Giranda VL, Heinz BA, Oliveira MA, et al. Acid-induced structural changes in human rhinovirus-14—possible role in uncoating, Proc Natl Acad Sci USA, 1992, vol. 89 (pg. 10213-7)
Corona viruses	<4.0	Alain Lamarre and, Pierre J. Talbot Effect of pH and temperature on the infectivity of human coronavirus 229E; Canadian Journal of Microbiology, 1989, 35(10): 972-974
Parainfluenza	<5	Hambling MH. Survival of the respiratory syncytial virus during storage under various conditions. Br J Exp Pathol. 1964;45(6):647-655.
Respiratory Syncytial Virus (RSV)	<6	Mol. Pharm. 2005, 2, 6, 491–499 Publication Date: September 14, 2005 https://doi.org/10.1021/mp0500465

4 TAFFIX PROOF OF CONCEPT STUDIES:

4.1 TAFFIX REDUCE INFECTION RISK BY 78% IN A SUPER-SPREAD EVENT.

The city of Bney Brak, Israel, (population 210,000 mostly ultra-orthodox Jews) tops Israel list of COVID-19 infection rate and mortality. In mid-September before the Jewish New Year (an intensive two day gathering for prayers) PCR positivity rates were 17.6% and those climbed to 28.1% two weeks later

In a prospective users survey, 243 members of a Jewish ultra-orthodox synagogue community in Bney Brak that participated in the two days holidays prayers (7 hours spent daily in the synagogue) were followed up for the following 14 days to measure the effect of Taffix in this potentially "super spread" (post mass gathering) event . 83 collected and used Taffix throughout Rosh Hashana prayers and for the following two weeks (intention to treat group, ITT) . 81 of them used it regularly as instructed (per protocol, PP) while two used it rarely if at all. The remaining 160 did not use Taffix .

At the end of the two weeks follow up - in the ITT population, 2/83 (2.4%) of the Taffix users and 16/160 (10%) of the Taffix non users were infected. The odds ratio for SARS-CoV-2 infection in Taffix users were 0.22 (0.05-0.99, Mid P exact =0.028), a reduction of 78% (95%CI 1%-95%) in odds of infection. No side effects were reported.

This is the first time that any measure to prevent infection in SARS-CoV-2 virus, beyond the use of masks. was proven effective.

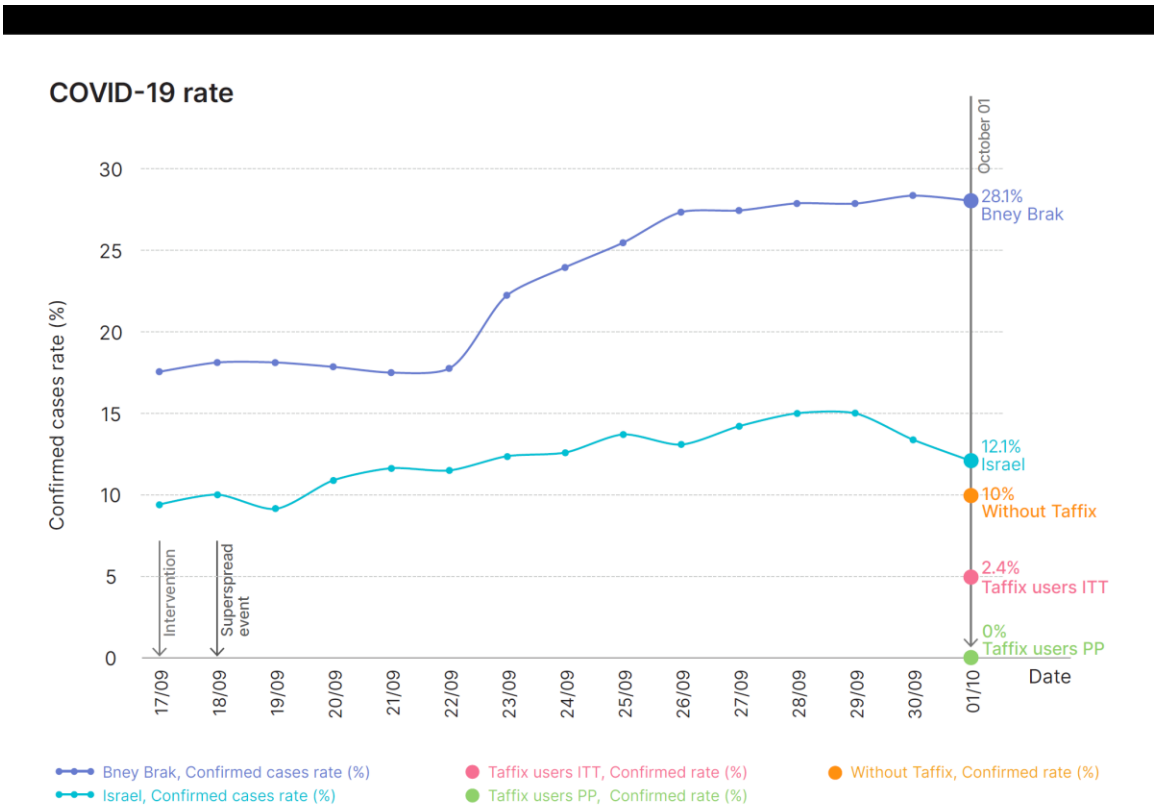

Figure 2: PCR positivity rate September 17- September 30

4.2 TAFFIX CREATES A STABLE GEL OVER NASAL MUCOSA

In an ex-vivo study (performed at Furmulex Pharmaceuticals ltd. Nes Ziona , Israel) 46 mg Taffix powder was sprayed into each single nostril of a pig's nose. (amounts were calculated to reflect the relative size of the pig's nose relative to an average human nose). The powder was slightly mixed with Instacoat color blue before spraying to allow for better visibility of the gel's integrity. The specimens were kept in an oven at 34C.

The gel was observed for integrity and gloss and photographed hourly for 6 hours. pH was measured in-situ at time 0 and at 6 hours.

The study showed that the gel is created within about a minute and remained intact for up to 6 hours. pH measured in situ was 3.6 at time zero and 4.4 at 6 hours.

Conclusion: Taffix creates a stable acidic gel immediately after its application on nasal mucosa and remains intact for up to 6 hours. The gel retains in situ low pH <4.4 for 6 hours.

Based on this study the recommendation to reapply Taffix every 5 hours if the user is still in a crowded area was determined.

4.3 TAFFIX IS ABLE TO PROTECT CELLS AGAINST INFECTION OF SARS-COV-2 VIRUS.

This study was performed at the University of Virginia Department of Medicine and Division of Infectious Diseases & International Health by Prof. Barbara Mann. [11]

The purpose of the study was to test whether the Taffix™ can form a protective barrier against SARS-CoV-2. A gel of *Taffix™* was performed on a 40 nm nylon filter, and then seeded with 10,000 PFUs of virus. An untreated filter, seeded with the same amount of virus, was used as an untreated control. After a 10-minute incubation the bottom of the filters were washed with culture media and then tested for live virus by plaque assay (Fig. 3) and for viral RNA using qRT- PCR (Fig. 4). Taffix™ reduced the amount of live viruses by more than 99%, and in most experiments no virus was detected or the amount of virus present was below the limit of detection of the assay in the undiluted flow through (Fig. 3). Using qRT-PCR techniques Taffix™ treatment reduced the amount of viral RNA by more than 4 logs (Fig. 4).

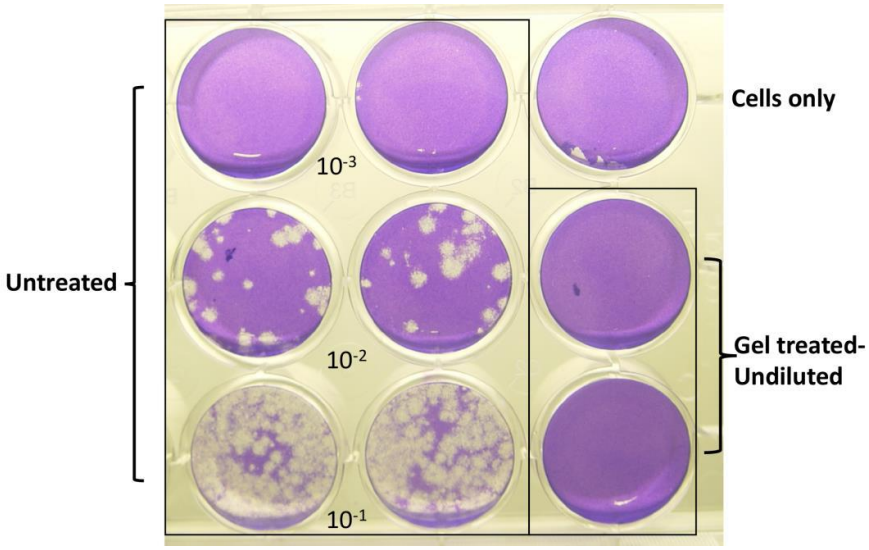

Figure 3:Plaque assays of flow through of Taffix™ gel-treated and untreated SARS-CoV-2.

Flow through from Taffix™ gel-treated without dilution and 10-1, 10-2 and 10-3 dilutions of untreated virus was added directly to tissue culture wells containing VeroE6 cells. Plates were incubated for two days before staining with crystal violet. Representative of 4 independent experiments.

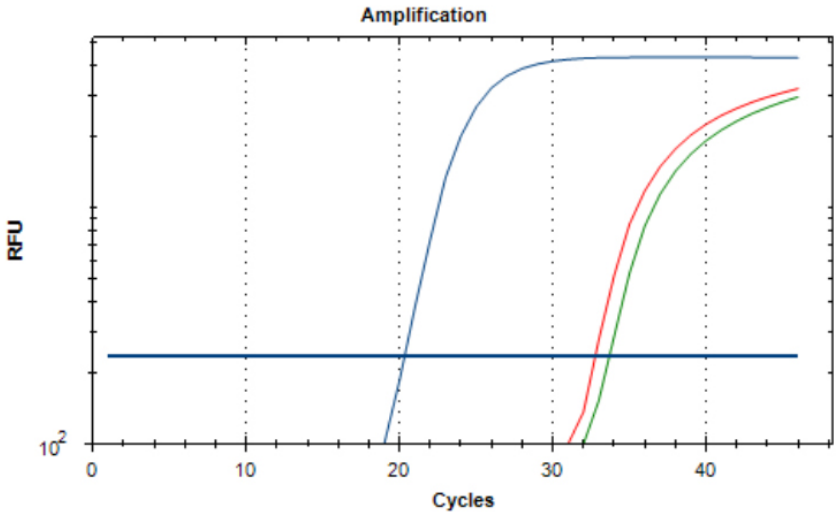

Figure 4: qRT-PCR of flow through of Taffix™ gel-treated and untreated SARS-CoV-2.

RNA from was isolated from flow through from Taffix™ gel-treated and untreated virus then converted to cDNA and amplified. Blue line is untreated, green the Taffix™ gel-treated and red is a plasmid DNA control. Representative of 2 independent experiments.

Conclusion: The gel layer produced by Taffix™ powder after administration of a clinical equivalent amount, effectively blocked SARS-CoV-2 virus, as demonstrated by reduction in virus RNA equivalent to 4 log reduction in virus count. Taffix™ also protected above 99% of cells from infection by live SARS-CoV-2 virus.

4.4 TAFFIX ACIDITY IS ABLE TO PROTECT CELLS FROM H1N1 INFLUENZA VIRUS:

The purpose of this study was to test the direct effect of the pH of different Taffix formulations on H1N1 virus's ability to reduce viability of MDCK cells.

MDCK cells were treated with various combinations of the Test Items alone, and virus pre-treated with the test items and controls. Cell viability was measured using a XTT.

T1	T2	Reference
Nasus HPMC A15 pH 3.5	Nasus HPMC A15 pH 7.9	"Nasaleze travel"

Results: Treatment of cells with saline only (1:10) significantly elevated cells' viability to 120% compared to untreated cells. Addition of virus to the cells significantly decreased their viability to 27% (a decrease of 93% when the virus was pre-incubated for 5 minutes with saline) and to 22% (a decrease of 98% when the virus was pre-incubated for 30 minutes with saline), compared to saline only treated cells.

• Treatment of cells with TI 1 only (Acidic) did not significantly affect cells' viability compared to untreated cells (viability was elevated to 107%). Addition of virus to the cells significantly decreased their viability only to 89% (a decrease of only 19% when the virus was pre-incubated for 5 minutes with TI 1) and to 90% (a decrease of 17% when the virus was pre-incubated for 30 minutes with TI 1), compared to TI 1 only treated cells.

• Treatment of cells with TI 2 only (Basic) significantly lowered cells' viability compared to untreated cells (viability was decreased to 43%). Addition of virus to the cells significantly decreased their viability to 35% (a decrease of only 8% when the virus was pre-incubated for 5 minutes with TI 2) and to 28% (a decrease of 15% when the virus was pre-incubated for 30 minutes with TI 2), compared to TI 2 only treated cells.

• Treatment of cells with Reference item only (Basic) lowered (not statistically significant) cells' viability compared to untreated cells (viability was decreased to 71%).

Addition of virus to the cells decreased their viability to 37% (a decrease of 34% when the virus was pre-incubated for 5 minutes with Reference item) and to 47% (a decrease of 24% when the virus was pre-incubated for 30 minutes with Reference item), compared to Reference item only treated cells.

• Tamiflu did not manage to recover cells viability following virus treatment.

Conclusion: Taffix Acidic formulation demonstrated significant protection against Influenza A (H1N1) virus in vitro.

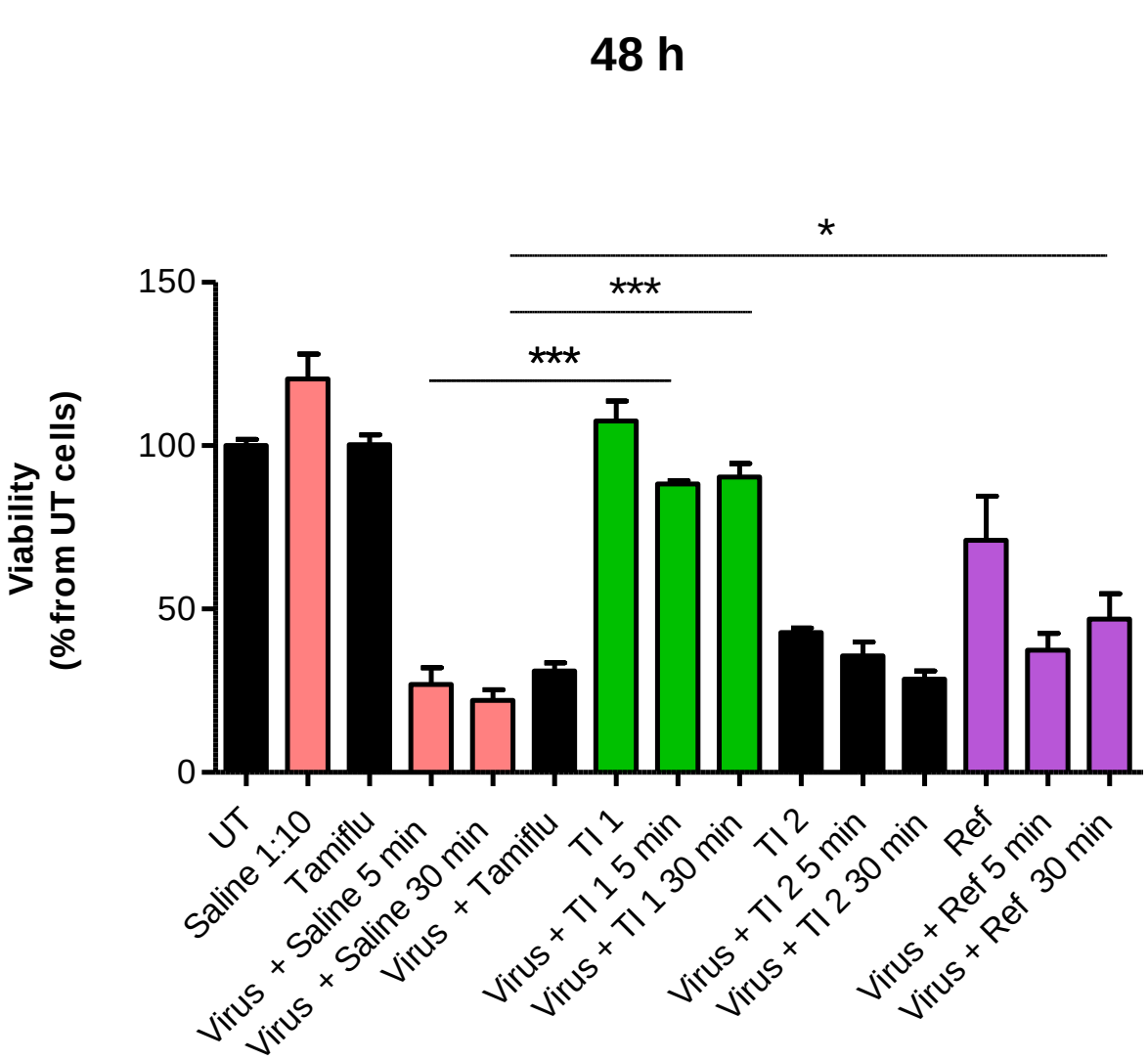

Figure 5: *Taffix is able to protect cell's viability when infected in pre-treated H1N1 Influenza virus*

MDCK cells were incubated for 48 hours with Test Items alone, Influenza A virus alone and various combination (pre-treatments of virus with Test Items). Cells' viability was determined by XTT viability assay. Results represent means ±SEM of wells in each group. *p<0.05, ***p<0.001 t-Test statistics are presented for each treatment with a Test Item alone compared to untreated cells, ##p<0.01, ###p<0.001, t-Test statistics are presented for each TI + virus treated cells compared to the relevant TI only treated cells. @p<0.05, @@@p<0.001 t-Test statistics are presented for each treatment of virus + TI compared to virus + saline at the same incubation timepoints, according to student's

4.5 TAFFIX GEL EFFECTIVELY PROTECTS CELLS FROM INFECTION OF LENTIVIRUS

In this study the barrier effect of the Taffix hydrogel formulation for viruses was investigated. The hydrogel was formed on in a cell strainer made from a nylon net with 40 µm holes. The primary aim was to determine if infective virus can pass through the test material. The secondary aim was to determine if virus trapped in the barrier remains active. Lentiviruses containing a green fluorescent reporter were used as a model virus.

The efficiency of the test-material (Taffix)l to act as a physical barrier for viruses was evaluated.

A lentiviruses was used as a model virus. This virus is approximately 100 nm in diameter and has an outer lipid bilayer. The lentivirus contains a GFP reporter gene and its presence in a solution can therefore be assayed through infection of standard cell-lines such as HEK293T.

Gels were formed by addition of the test-material in powder-form on top of a highly porous net. The gels were challenged with a solution containing the lentivirus. The solution was applied in minimal liquid volume (10 µl), in order to not dissolve the film. At predetermined time-points the liquid that passed through the gel was removed by washing to determine if active virus had passed through the gel. Thereafter the gel was dissolved in order to determine if active virus remains in the gel.

The quantity of active virus in the different phases (media, film, hydrogel) were determined by infection studies using HEK293T. Solutions from the different phases were added to cultured cells and remaining infectious virus in respective solution were detected by expression of GFP

The results of this study indicate that 97% of the lentiviruses were not able to cross the Taffix gel and infect cells (Figures 9 and 10 , infected cells are fluorescent).

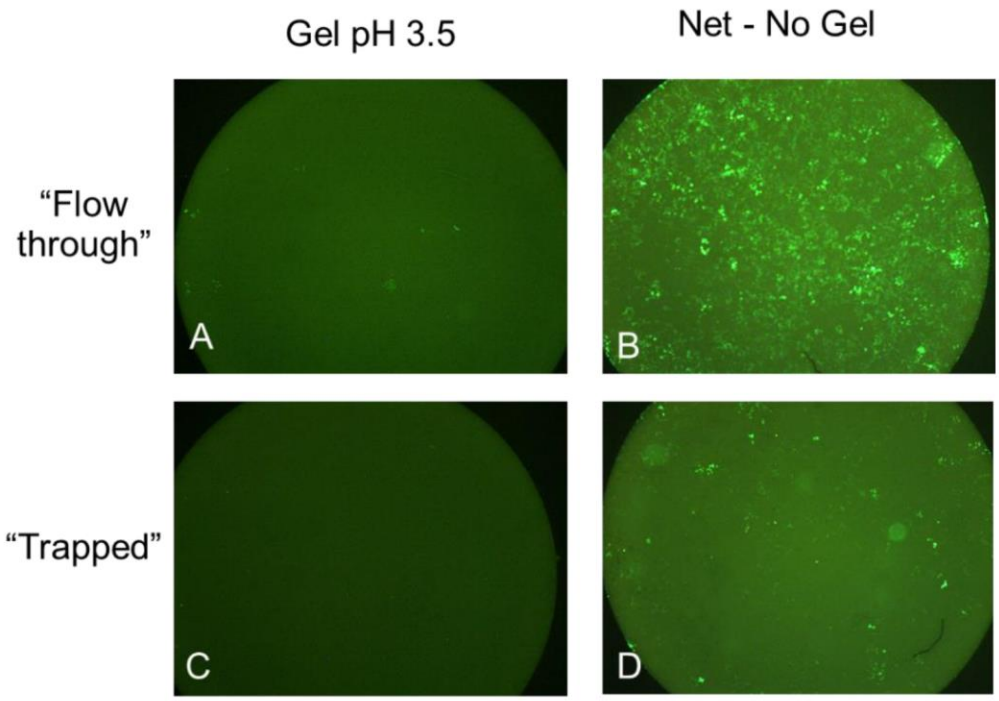

Figure 6: Microscopy results of Lentivirus

Fluorescence indicate the presence of viruses. Flow-through is material collected below gel after incubation. A- Where viruses are added to gel almost no signal is detected in flowthrough. B- Without gel a strong signal is detected. "Trapped" is the dissolved gel. C- No active virus is detected in the dissolved gel. D- Some virus can be detected on the Net by intense washing.

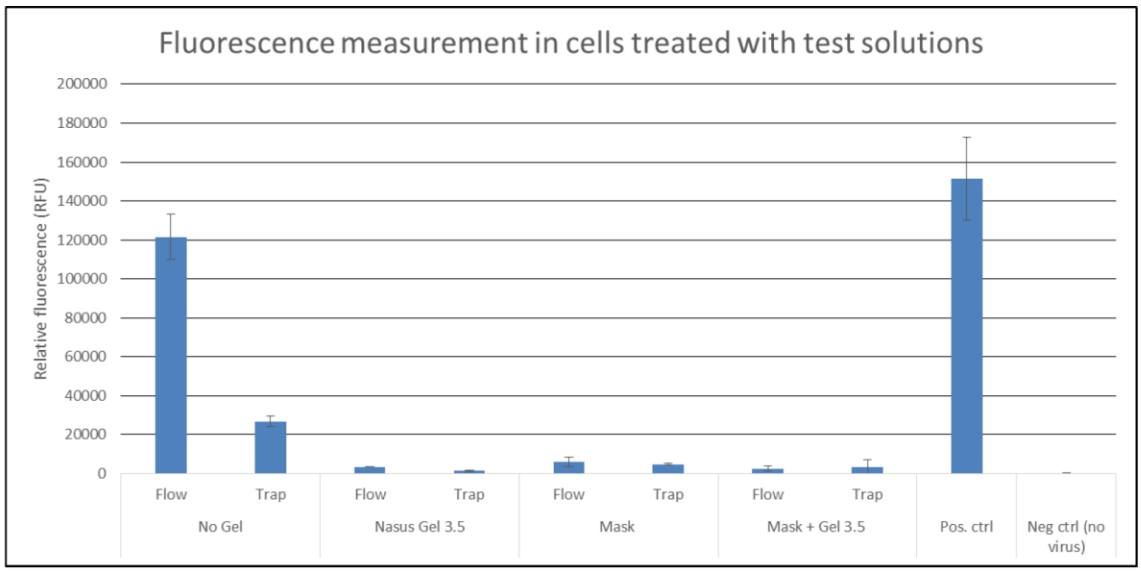

Figure 7 :Fluorescence measurement Lentivirus study

No gel sample fluorescence is primarily detected in the Flow through fraction. Some active viruses remained in the net. Total activity is decreased compared to positive ctrl. Nasus Gel decreases fluorescence intensity in "Flow fraction" to noise level

Conclusion: Protecting cells in Taffix against Lentivirus model reduced virus infectivity to noise level ~3%. The effectivity of Taffix gel in blocking the virus was 97%.

5 SUMMARY POC

The concept of effective extracellular blocking of viruses over the nasal mucosa with low pH gel has been described and well validated in the scientific literature as a useful mean to block respiratory virus infections with many respiratory viruses. Taffix was proven to successfully create a low pH microenvironment in the nasal cavity and prevents viruses from reaching the cells and infecting them.

More important: real life experience ahead of a mass gathering (super spread) event showed that Taffix has unprecedent protective effect, reducing infection risk four fold. Such an effect was never described before for any other preventive measure.

As a safe and effective additional layer of protection (in addition to all recommended measures including masks) Taffix has an important place in preventing viral respiratory infections and specifically for the current COVID19 disease.

NASUS PHARMA

Ministry of Health
Medical Technology, Information and Research Division
Medical Devices Department

מדינת ישראל
STATE OF ISRAEL

משרד הבריאות
טיבת טכנולוגיות רפואיות, מידע ומחקר
גף ציוד רפואי

אישור רישום בפנקס הציוד הרפואי

ניתן בזאת אישור , כי בהתאם לבקשת רישום מס : 33010001
הציוד הרפואי (אביזרים / מכשירים רפואים (אמ"ר)) הבא :

שם הציוד הרפואי	TAFFIX טאפיX
קבוצות	1. Nasus Nasal (Powder) Spray Device 2. Alternative names: TAFFI, Preventus, V-Shield, Vir- protect, AF-Virus
יעוד הציוד הרפואי	The Nasus Nasal (Powder) Spray Device is intended for use to block inhaled viruses and bacteria within the nasal cavity.
התויה	1. אף אוזן גרון - The Nasus Nasal (Powder) Spray Device is indicated for use to block inhaled viruses within the nasal cavity.
שם בעל הרישום וכתובתו	NASUS PHARMA LTD ; הרכבת 29 תל אביב, ישראל ; ISRAEL
שם היצרן וכתובתו	Nasus Pharma Ltd. ; Haracevet 29 Tel Aviv ; ISRAEL
שם אתר היצור וכתובתו	1. F&C Licorice Ltd. - 1 Hayahalom St., Kiryat Shmona - ISRAEL

Certificate of CE-Registration

mdiEuropa

This is to certify that, in accordance with either medical device Directive 93/42/EEC as amended by 2007/47/EC or Directive 98/79/EC, mdi Europa GmbH agree to perform all duties and responsibilities as the Authorized Representative for

Nasus Pharma Ltd.
Harakevet 29
6618306 Tel Aviv
Israel

as stipulated and demanded by the afore-mentioned Directives. The German competent authorities have allocated the medical devices of the manufacturer the following registration numbers:

GMDN Code	Description	Classification	Registration Number
45592	Nasal air filter	I	DE/CA09/0760/N18/001

The manufacturer has provided mdi Europa with all necessary documentation, together with an appropriate Declaration of Conformity confirming that the medical devices fulfill the essential requirements of either Directive 93/42/EEC as amended by 2007/47/EC or 98/79/EC. A safety officer has been appointed for Germany and therefore is in full compliance with § 31 MPG.

Signed on 08 May 2020

Werner Sander
President

TAFFI

REF TBD

Intended Use

The Nasus Nasal Spray Device is intended for use to remove particles from the air for medical purposes. The Nasus Nasal Spray Device is intended for Over-The-Counter Use.

Indication for Use

The Nasus Nasal Spray Device is indicated for use as a protective mechanical barrier against allergens and viruses (e.g., SARS-CoV-2) within the nasal cavity.

When to use TAFFI

To protect against airborne viruses, **TAFFI** should be used prior to exposure to allergens and a high risk environment where viruses may be airborne, such as public place (e.g., supermarkets, pharmacies) or encounters with anyone outside of the isolated members of the household.

TAFFI may be applied **up to 3 times** over the course of the day.

How does TAFFI work?

TAFFI is a powder nasal spray, the powder turns to a gel in the nose which creates a barrier to protect against allergens and airborne viruses.

If concurrent use of another nasal spray is required, **TAFFI** should be re-applied afterwards so that the barrier created is not disturbed.

TAFFI can be used in addition to other treatments, as part of combination therapy strategy in the fight against allergies and viruses. For example, **TAFFI** may be used in addition to donning a mask and wearing gloves.

Who can use TAFFI?

- **TAFFI** is suitable for adults, athletes, and children from 12 years old.
- **TAFFI** does not contain any drugs or medicines.
- **TAFFI** has a good safety profile.
- **TAFFI** is non-drowsy.

Contraindications

- Children under 12, consult a physician.
- If pregnant or breast-feeding, consult a physician.
- Do not use this product if you are sensitive to cellulose or citric acid.

Cautions:

- **Discard TAFFI bottle on the expiration date printed on the bottle or 1 month after first opening - whichever comes first.**
- **To avoid contamination do not use this product for more than one person.**
- **May be used up to 3 times a day.**

- Keep out of reach of young children.
- Avoid contact with open wounds.
- Avoid contact with eyes.
- If powder gets into your eye, rinse with water.
- Do not rinse the bottle with water or other liquid as this may block the bottle.
- Do not use if tamper evident seal is broken.
- Always close the cap.
- Very few cases of allergic reactions to this product have been reported. Most reports received have been blocked nose, runny nose, sneezing, sore throat. If you experience reactions more severe that this then use of the product should be discontinued immediately and if symptoms persist, consult your physician.

How to store TAFFI

- Store at room temperature (or between 5°c and 30 °c (41°F ~ 86°F).
- Do not refrigerate or freeze.

How to use TAFFI

To defend against airborne allergens and viruses, **TAFFI** may be applied up to 3 times per day to maintain an effective barrier. Once applied, **TAFFI** is effective for approximately 5-6 hours.

Remember- TAFFI bottles cannot be shared with other people. Mark your bottle and avoid sharing it with other people to prevent potential transmission of viruses or germs

Step 1 – Blow your nose.

Step 2 – Shake the bottle twice

Step 3 – Place the nozzle of the bottle just inside the nose and apply 1 to 2 sprays into each nostril. Inhale gently while squeezing but do not inhale deeply.

Step 4 – wipe the bottle with a fresh cleaning wipe to maintain hygiene.

During first use, you may experience a tingling or burning sensation in the nose or light sneezing. This is a transient sensation that will go away as you become used to using **TAFFI.**

You may also feel some form of irritation, especially if your nasal membranes are already inflamed or irritated. This will subside quickly.

Some individuals can feel a slight sensation or blocked nose, this is normal and is the feel of the barrier created by **TAFFI.** If you experience continuous discomfort you can wash your nose with warm water until relief. If you experience serious discomfort after application of **TAFFI** consult your physician.

TAFFI bottle should be used for one person only, sharing a bottle with other people could expose them to infection!!

Chemical Composition: Hypromellose (HPMC) (89.9%), Citric Acid (6%), Sodium Citrate (4%), Benzalkonium Chloride (0.1%) and Menthol (<0.1%).

Symbols Glossary:

	Legal Manufacturer	EC REP	Authorized representative in the European Community
CE	CE Mark, indicating that the device complies with Council Directive 93/42/EC (MDD)		Do not use if package is damaged
	Caution, consult accompanying documents	°C	Minimum and maximum storage temperatures
	Consult instructions for use		Keep away from sunlight
LOT	Batch Number		Expiry date (In format: YYYY-MM-DD)
REF	Catalogue number		Keep dry

Manufacturer:
Nasus Pharma Ltd.
Harakevet 29 Tel Aviv, 6618306, Israel
Tel: +9723-573-6632
Fax: +9723-573-6664
Email: info@nasuspharma.com
Website: nasus.com
Made in Israel

CE

Registration number In Israel MOH (AMAR): 33010001

EC REP

Mdi Europa GmbH
Langenhagener Str. 71, D-30855 Langenhagen, Germany
Tel: +49 511 39089530
Email: info@mdi-europa.com
Website: mdi-europa.com

IFU-0001-EN Rev. 1.0 04/2020

[1] US Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): situation summary. Accessed March 15, 2020. https://www.cdc.gov/coronavirus/2019-ncov/summary.html

[2]. https://www.cdc.gov/coronavirus/2019-ncov/prepare/transmission.html accessed March 16 2020.

[3] Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. *JAMA.* Published online March 11, 2020. doi:10.1001/jama.2020.3786

[4] Sungnak W, Huang N, Bécavin C, et al. SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes. *Nat Med*. 2020;26(5):681-687. doi:10.1038/s41591-020-0868-6

[5] Hou YJ, Okuda K, Edwards CE, et al. SARS-CoV-2 Reverse Genetics Reveals a Variable Infection Gradient in the Respiratory Tract [published online ahead of print, 2020 May 27]. *Cell*. 2020;S0092-8674(20)30675-9. doi:10.1016/j.cell.2020.05.042

[6] Hayden FG, Treanor JJ, Betts RF, Lobo M, Esinhart JD, Hussey EK. Safety and Efficacy of the Neuraminidase Inhibitor GG167 in Experimental Human Influenza. *JAMA.* 1996;275(4):295–299. doi:10.1001/jama.1996.03530280047035

[7] Hull D, Rennie P, Noronha A, et al. Effects of creating a non-specific, virus-hostile environment in the nasopharynx on symptoms and duration of common cold. *Acta Otorhinolaryngol Ital*. 2007;27(2):73-77.

[8] Gern JE, Mosser AG, Swenson CA, et al. Inhibition of rhinovirus replication in vitro and in vivo by acid-buffered saline. *J Infect Dis*. 2007;195(8):1137-1143. doi:10.1086/512858

[9] Rennie P, Bowtell P, Hull D, Charbonneau D, Lambkin-Williams R, Oxford J. Low pH gel intranasal sprays inactivate influenza viruses in vitro and protect ferrets against influenza infection. *Respir Res*. 2007;8(1):38. Published 2007 May 17. doi:10.1186/1465-9921-8-38

[10] Adapted from Monto AS: Epidemiology of viral respiratory infections. Am J Med, 2002 Apr 22;112 Suppl 6A:4S-12S

[11] Preprint before publication . available at UVA.