

1 **Low pH Hypromellose (Taffix™) nasal powder spray reduced SARS-CoV-2**
2 **infection rate post mass-gathering event at a highly endemic community: An**
3 **observational prospective open label user survey**

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12 Keywords: SARS-CoV-2, COVID 19, Prevention, Hypromellose, Nasal spray, H1N1,
13 low pH, respiratory viral infection)

14 Word count: Abstract 337

15 Word count: Main text 2568

16 Short Title: Low pH Hypromellose (Taffix) nasal powder spray reduced SARS CoV 2
17 infection rate . An observational prospective open label user survey.

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31 Abstract:

32

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

37 Taffix - is an innovative nasal powder inhaler that creates a protective gel layer over the
38 nasal mucosa and effectively blocks viruses from infecting the nasal cells. Taffix is
39 approved for use in Europe and Israel. In vitro studies demonstrated that Taffix blocks
40 viruses (including SARS- CoV-2) from infecting human cells (<99%). It is well
41 established that the nose is the main gateway of SARS- CoV-2 to the body. Taffix™ was
42 developed as an additional virus protective tool beyond the currently recommended
43 preventive measures.

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

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

56 **Conclusion:** We suggest that Taffix can be an additional powerful tool against COVID19
57 spread. To our knowledge this is the first time that any measure to prevent infection in
58 SARS-CoV-2 virus, beyond the use of masks. was proven effective.

59

60 Introduction

61 Following a sharp decline in SARS-CoV-2 incidence during May 2020, Israel suffered a
62 gradual increase in the number of cases on June-July and a sharp increase in August [1]
63 On September 18 2020, Israel was a world leader in the number of new COVID-19 cases
64 per million citizens. The infection rate among its ultra-orthodox communities was double
65 that of the general population. On September 30th there were 23.6 confirmed COVID-19
66 patients per 1000 citizens in Bney Brak, and a total of 4741 active confirmed cases.

67 Since the beginning of the pandemic in Israel 18,743 Bney Brak citizens contracted the
68 disease that cost the lives of 80 individuals. (as of September 29 2020) Of note the
69 mortality rate in Israel is 182 per million citizens while the calculated mortality in Bney
70 Brak is more than double that: 380 per million.

71 During September, Jewish high holydays are characterized by mass gatherings and
72 prayers. Of special concern as a source of additional spread of the disease were Rosh
73 Hashana (the Jewish New Year) prayers: a two- days holiday that is spent mostly in
74 synagogues and in large family gatherings. In 2020 Rosh Hashana began on the evening
75 of September 18 and lasted for two days ending in large celebrations involving big
76 crowds. This event raised concern as a potential post-mass gathering outbreak.

77 Indeed, in mid- September just before Rosh Hashana (Jewish New Year) there were
78 about 17.6% positivity rates in the city of Bney Brak, and those actually climbed to
79 28.1% two weeks later [2] A similar trend was identified in other ultra-orthodox
80 communities both in Israel and in greater NYC [3].

81 Viral entry through the nasal mucosa is considered a main mechanism in SARS-CoV-2
82 infection [4]. Taffix's main ingredient- Hydroxypropyl methyl cellulose, (Hypromellose
83 or HPMC) is a muco-adhesive gel-forming cellulose derivative. Upon reaching the nasal
84 mucosa HPMC is known to absorb fluids and create a micron-sized gel [5] that covers
85 the nasal cells and prevents viruses from engaging with the receptors that are necessary
86 for the viral penetration into the cells. Additionally, Taffix creates a local acidic
87 microenvironment of pH 3.5 on mucosal surfaces, which remains stable for up to 5 hours.
88 An acidic microenvironment in the nose was shown to prevent multiple respiratory
89 viruses such as N1H1 influenza and Rhinoviruses [6] and recently SARS-CoV-2 [7] from
90 infecting cells.

91 Taffix™ - is an acidified Hypromellose nasal powder spray inhaler approved for sale and
92 used for prevention of respiratory viral infections. Taffix™ received CE marketing
93 approval (DE/CA09/0760/N18/001) and the Israeli Ministry of Health marketing
94 authorization (Amar- 33010001) and other countries. Taffix is sold in Israel since early
95 July 2020 reaching tens of thousands of users. No reports of adverse events were
96 registered in the post marketing database kept in compliance with regulatory requirement.

97 To assess real-life effect of Taffix in reducing SARS-CoV-2 infection rates following the
98 mass social gathering in closed environment during the Rosh Hashana holiday, we
99 conducted a prospective user survey at an ultra-orthodox synagogue in Bney Brak, a
100 highly endemic community.

101 Material and methods

102 Taffix has been tested in two in vitro studies to gauge its effectivity in blocking and
103 disabling respiratory viruses SARS-CoV-2 and H1N1 influenza.

104 The purpose of the study of the SARS-CoV-2 study was to test whether the Taffix™ can
105 form a protective barrier against this virus. A gel of Taffix™ was formed on a 40 um
106 nylon filter, and then seeded with 10,000 PFUs of virus. An untreated filter, seeded with
107 the same amount of virus, was used as an untreated control. After a 10 minute incubation
108 the bottom of the filters were washed with culture media and then tested for live virus by
109 plaque assay and for viral RNA using qRT-PCR Taffix™ reduced the amount of live
110 viruses by more than 99%, and in most experiments no virus was detected or the amount
111 of virus present was below the limit of detection of the assay in the undiluted flow
112 through. Using qRT-PCR techniques Taffix™ treatment reduced the amount of viral
113 RNA by more than 4 logs [7] The purpose of the H1N1 study was to test the direct effect
114 of the pH of different Taffix formulations on H1N1 virus' ability to reduce the viability
115 of MDCK cells. MDCK cells were treated with saline, Hypromellose, or Taffix with or
116 without virus. Cell viability was measured using a cell proliferation assay kit (XTT
117 based).

118 H1N1 virus pretreated with saline for 5 minutes reduced cell viability to 27%.
119 Pretreatment of viruses with Hypromellose alone (pH-6.8) reduced cell viability to 37%
120 while pretreatment of viruses with Taffix for 5 minutes resulted in 88% cell viability,
121 attesting to ability of Taffix to disable aggressive respiratory viruses [7].

122 We collaborated with a medium sized synagogue community comprising of some 250
123 members. After a preliminary notification members of the community expressed their
124 interest in using Taffix throughout Rosh Hashana prayers and the following two weeks.
125 Critical to the cooperation of the community members and their individual compliance,
126 was the strong support and encouragement of the spiritual leadership of the community:
127 the Rabbi and the wardens (Gabbaim). Typically, in ultra-orthodox communities – this
128 community is very close knit and its members are well familiar with each other as well as
129 to well known to the leaders of the community. The synagogue serves as the center
130 around which the community day lives revolves. Importantly, it was clarified that Taffix
131 offers an extra layer of protection and does not replace the mandatory use of masks. This
132 was clearly and repeatedly explained to all participants.

133 Each member was eligible to collect a Taffix bottle at the synagogue the day before Rosh
134 Hashana prayer and received written instruction on the proper usage of the device.
135 Family members residing in the same house hold were also eligible to receive Taffix
136 bottles (one each). Members also committed when they signed up to receive Taffix to use
137 it whenever encountering a large social interaction and reapply it every five hours
138 whenever they were leaving their residence for the following two weeks. Weekly
139 reminders to all participants were sent directly through the community email system and
140 close attention and monitoring was carried out to substantiate the number of confirmed (
141 PCR tests offered freely in the city) new cases in the community.

142 By the 14 day after the Rosh Hashana holiday the wardens of the synagogue followed up
143 each family with a personal phone interview. Members and their families were asked to
144 report whether they have used Taffix, how often and under what circumstances they used
145 it, and whether there were new cases of COVID-19 infection since Rosh Hashana,
146 Information about the total number of confirmed new COVID-19 cases in the rest of the
147 community was also collected and confirmed. Confirmed case were defined as all
148 SARS-CoV-2 PCR positive cases during days 1-14 of the follow up period. PCR testing
149 was offered freely at Bney Brak citizens in that period.

150 Statistical methods

151 The analysis of the results was performed first on the ITT (Intent-to-treat) population data
152 (All members who used Taffix) and then on the PP (Per-Protocol) population. (members
153 who used Taffix regularly according to instruction)

154 The Fisher's exact test for the comparison of two proportions (from independent
155 samples), expressed as a percentage, was applied to compare the contagion rate between
156 Taffix users and none users.

157 Fisher's exact test is used to calculate an exact P-value for a 2x2 frequency table with
158 small number of expected frequencies.

159 All tests are two-tailed, and a p-value of 5% or less is considered statistically significant

160 The data was analyzed using the SAS ® version 9.4 (SAS Institute, Cary North
161 Carolina).

162 Results:

163 Overall, 243 members of the Synagogue participated in the two days holidays prayers (at
164 least seven hours spent in the synagogue each day in a closed room). The day before
165 Rosh HaShana 113 Taffix bottles were collected. Of the 243 members, 83 (34%), men
166 women and children above the age of 12 years, (as per Taffix indication) reported Taffix
167 use, of which 81 (98%) reported per protocol use instructed before entering a populated
168 area and every 5 hours. Two (2%) members used Taffix “once or twice” throughout the

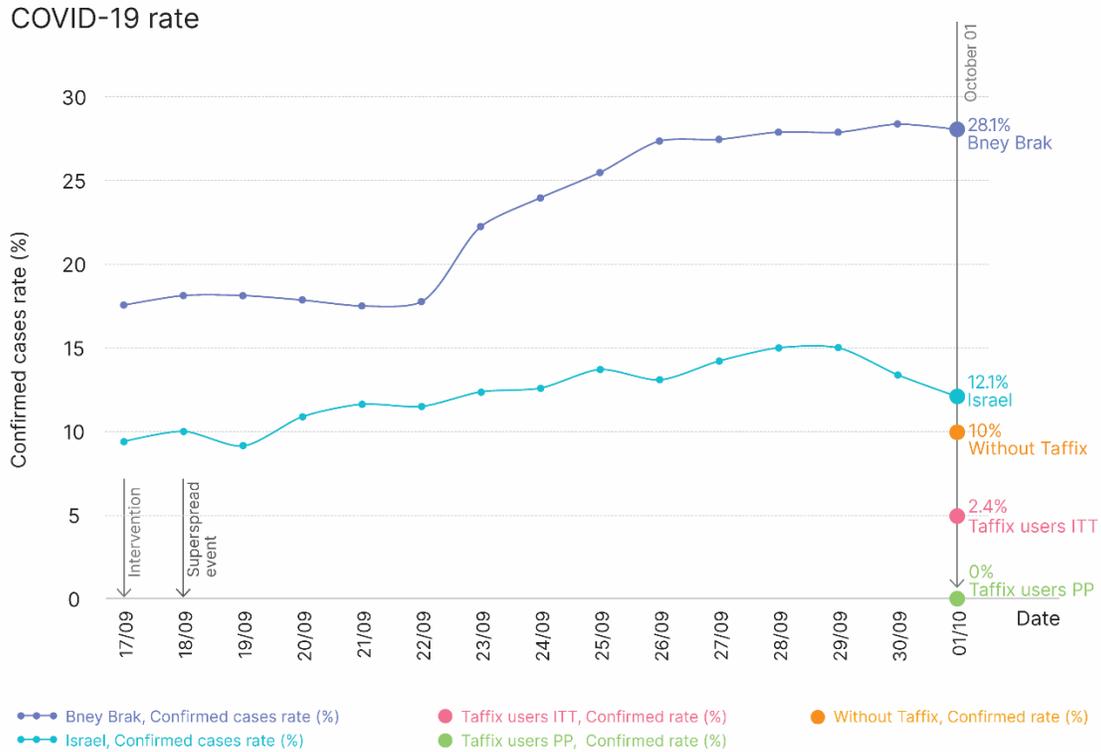
169 14 days period. There were no reports of side effects and most users commented on the
170 ease of use and had no problem in adapting the use of Taffix to their daily routine. 160
171 (66%) members of the community from this population of families, either did not
172 collect the Taffix at all or collected it and did not use it at all, not even once.

173 Of 243 members of the community, eighteen (7%) were confirmed as new SARS-CoV-2
174 infections during the 14 days following Rosh Hashana: Among the eighteen new
175 confirmed cases sixteen (89%) of them did not collect or used Taffix, two (11%)
176 collected Taffix but did not adhere to recommended use, that being only once or twice
177 throughout the whole two weeks period. One of them was diagnosed 2 days after Rosh
178 Hashana (possibly exposed prior to the beginning of the survey). All 81 members who
179 used Taffix regularly according to the instruction for use were not infected at all during
180 the study period of 14 days following Rosh Hashana.

181 In the ITT population, 2/83 (2.4%) of Taffix users and 16/160 (10%) of Taffix non users
182 were infected. The odds ratio for SARS-CoV-2 infection in Taffix users were 0.22 (0.05-
183 0.99, Mid P exact =0.028) and therefore a reduction of 78% (95%CI 1%-95%) in odds of
184 infection.

185 In the PP population, 0/81 (0%) of the Taffix users and 16/160 (10%) of the Taffix non
186 users were infected. The odds ratio for SARS-CoV-2 infection in Taffix users were 0
187 (0.00-0.38, Mid P exact <0.001).

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191 Figure 1 Rate of positive SARS-CoV-2 PCR tests in the city of Bney Brak and in Israel
 192 following mass gathering events on Jewish New Year, September 18- October 1st.

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194 Discussion

195 We conducted a prospective user survey in a densely populated city, during peak
196 epidemic period with high incidence of transmission ahead of what was perceived to be a
197 super-spreading event during the Jewish Rosh Hashana prayers. Users reported no
198 adverse effects and a substantially lower infection rates compared with persons from the
199 same community with similar exposure. This significant reduction despite high risk
200 exposure suggests significant effectiveness of Taffix in prevention of SARS-CoV-2
201 infection and reduction of above 4 fold in the risk of infection. Of note in this time period
202 the number of new cases in the city of Bney Brak increased by 1.6 folds as positivity
203 rates went from 17.6% to 28.4.

204 Taffix is an acidified Hypromellose powder nasal spray. Upon reaching the nasal mucosa
205 Taffix absorbs water and creates an even micron-sized gel that lasts about 5 hours. This
206 gel creates low pH microenvironment on the nasal mucosa that was proven to prevent
207 viruses from reaching nasal cells and infecting them. In the context of the SARS-CoV-2
208 epidemic it has been proven that cells of nasal mucosa are the main gateway of viruses
209 into the body and the need to protect the nose is now widely accepted. Taffix is
210 commercially available both in Israel and in Europe as well as other countries in South
211 America and Asia. Based on prior in vitro studies conducted by the developers that
212 showed high viricidal activity of the Taffix we conducted a prospective users survey to
213 gauge the real life effect of Taffix in preventing further outbreak of COVID 19 disease
214 before an event that involved mass gathering of people.

215 Our results could be influenced by selection bias whereby people who were more
216 concerned about the possibility of infection would choose to use any additional protection
217 offered to them and might be more careful in observing social distancing and use of
218 masks.

219 While this certainly is a possibility several points should be considered: 1. At this
220 synagogue members could not enter or remain indoors without properly wearing a mask
221 throughout the whole of the services. The prayer room was divided to “capsules” and
222 every effort was made to prevent mingling of people beyond their allocated capsule. 2.
223 Even in countries where the use of masks and social distancing was adhered to and
224 enforced- the infection rate dropped dramatically but did not reach anything near zero
225 infection rate– attesting the relative but not absolute protection of these measures [8].3.
226 On a community level even reducing infection rate among people who are more aware of
227 the risks and are not fully protected due to the limitation of the current safety measures
228 and extremely high prevalence in the community- can significantly lower the numbers of
229 patients and the risks associated with contracting the disease. 4. These results suggest
230 further that Taffix provided protection to people who used it as instructed, not only in the
231 community gathering but also at home, where they did not wear a mask, even when they
232 had an infected family member leaving in the same household.

233 Additional limitation of this user survey might be the relatively small size of the
234 community and lack of information on the different demographics of the ITT and the
235 non-users populations. These are inherent to the use of post marketing survey. Obviously,
236 a prospective clinical study will enrich our understanding of the relative efficacy and the
237 specific circumstances where Taffix will be most efficient in preventing infection. That
238 being said the results of this user survey indicate that among users of Taffix there was a
239 significantly lower infection rate with SARS-CoV-2 infection.

240 Conclusion

241 Out prospective user survey showed lower SARS-CoV-2 infection rates in Taffix users
242 during a high risk mass gathering. No adverse events were reported. further evaluation by
243 controlled clinical trials is warranted to confirm its findings and define ways to encourage
244 better compliance.

245 To our knowledge this is the first time that any measure to prevent infection in SARS-
246 CoV-2 virus was proven effective beyond the use of masks. Given the excellent safety
247 profile of Taffix and its statistically significant efficacy in preventing infection following
248 what is defined as high risk infection event - it seems that this additional layer of
249 protection can significantly reduce the risks of infection and may enable people to
250 resume some part of their daily routine more safely. While many countries in the world
251 are still struggling to control the epidemic and others are nearing a second wave and
252 additional lockdown- these finding could indeed raise some hope and be added to our
253 meagre arsenal against the SARS-CoV-2.

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259 Statement of Ethics:

260 This is a user's survey of a commercially available product and as such ethical approval
261 was not required or obtained, All participants signed a consent form and received full
262 user instructions.

263 Conflict of Interest Statement and funding:

264 DM and TL are employees of Nasus Pharma. BM conducted Nasus Pharma funded
265 preclinical research at the University of Virginia. Nasus Pharma donated Taffix to the
266 participants.

267 Author Contributions.:

268 SK and YN developed the study protocol and participated in the analysis of the results
269 and the written manuscript

270 DM and TL developed the study protocol and participated in the analysis of the results
271 and the written manuscript as well as in the follow up and operation of the study

272 BM researched the preclinical POC of Taffix with SARS-CoV-2 .

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