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Research Article

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Virucidals Control the Presence of Covid in Mouth/Saliva

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Abstract

Summary: *This pilot study evaluated the effects of some virucidals in vivo (RT-PCR swab test) to define the presence of COVID in the mouth saliva. With this model, if an asymptomatic subject is positive (in the mouth saliva, the first incubating medium), virucidals may be used and the positivity can re-evaluated to define their viral killing power.*

Results: *A progressive decrease in positivity in the swab samples was observed. Virucidals' produced disappearance of positivity in most subjects at 3 days. All virucidals used in this pilot registry resulted effective. The pharmaceutical form seems to be important to assure persisting traces of the virucidal in the mouth. Phyrorelief possibly produced the longest action (>3 hours) due to its slower release. These observations indicate a significant effect of virucidals on the viral contamination of the mouth with a simple, cost-effective model. The lower presence of a virus charge may reduce contagiousness of most patients and possibly, the spread of viral material from the mouth. The effects on the evolution of COVID-19 on single patients is, unknown but virucidals may assume a significant community value in controlling spreading.*

Keywords: Covid, Virucidals, Virus, Salivary Glands Virosis, Saliva, Contagion, Contagiousness

Introduction

Covid swabs detect the presence of COVID elements in saliva. The test is simple and fast but not completely reliable from a diagnostic point of view (one patient can be negative today and positive tomorrow). Testing identifies the SARS-CoV-2 virus and detect the presence of viruses (RT-PCR, isothermal nucleic acid amplification, and antigen) or the presence of antibodies.

The real-time reverse transcription polymerase chain reaction (rRT-PCR) test can be done on respiratory samples (including a nasopharyngeal swab or saliva/sputum samples) [1-3]. Results are generally available within hours. The presence of viruses in saliva is a significant source of contagion; the oropharyngeal cavity is considered the real human incubator and the viruses multiply until they reach a critical mass to spread to target organs (trachea, bronchial tree and lungs). The salivary glands may also host the virus and operate as a secondary incubator; this may be linked to super spreading with prolonged release of viruses and sustained contagiousness. This registry evaluated the effects of some virucidals in vivo (using the RT-PCR test) to evaluate the presence of COVID in the saliva. With this model, if an asymptomatic subject is positive (in the mouth saliva, the first incubating medium), virucidals can be used, i.e., for a week, and the positivity re-evaluated to define the direct killing power of the virucidal.

Presence of the Covid-19 Virus in Saliva and in Salival Glands

Viral elements in saliva – the main incubator – is possibly associated to super spreading. In most of these subjects COVID-19 symptoms may be very mild (i.e., submandibular pain, swelling at the parotid and submandibular glands, sublingual glands, dry mouth, difficult swallowing). Salivary gland virosis may be very persisting for example with cytomegalovirus infection.

Methods, Subjects

Asymptomatic 'patients' (found as positive) who were otherwise healthy were evaluated. Their age was <55. No drugs had been used, a normal oral hygiene was regularly observed, their body temperature was normal. The test was made before 10 am, without washing mouth or teeth and without breakfast. The same tests were repeated at 3 days under similar conditions. No specific drugs were used during the observation period and no significant symptoms occurred or were reported. All subjects remained asymptomatic. Progression to symptoms and to need for management or hospitalization for COVID-19 (or any other condition) was considered an exclusion item. All subjects respected the anti-viral measures (mask, hygiene, distancing) and used Vitamin C and a normal diet. Virucidals are generally available without prescriptions. Products, commonly available as Over the Counter (OTC) were used.

PhytoRelief: (Alchem) includes pomegranate (as the main local virucidal/antiviral) in association with ginger and turmeric.

Pomegranate extract is one of the most powerful natural antivirals. The lozenge is slowly dissolved in the mouth; its effects may last more than 3 hours. The product includes, with pomegranate, elements considered both virucidals and anti-virals (if used for systemic administration).

Benzydamine: (Also known as, Tantum Green branded in some countries as Difflam or Septabene), is available as the hydrochloride salt in a solution. It is a locally acting nonsteroidal anti-inflammatory drug (NSAID) with local anesthetic and analgesic properties for pain relief and anti-inflammatory treatment of mild conditions of the mouth/upper throat.

Baicalin (85%) (Obtained by InXi, Shanghai). This product (alone or in combinations) has been diffusely used in Wuhan during the epidemic (however, data are not accessible). It is a flavone glycoside (the glucuronide of baicalein). This product is an Inhibitor of 5- and platelet 12-lipoxygenases (IC50 values are 9.5 and 0.12 μM respectively). It also inhibits Raf-mediated MEK-1 phosphorylation in glioma cells and induces G1 and G2 cell cycle arrest by decreasing cdk1, cdk2, cyclin D2 and cyclin an expression. Baicalin inhibits the production of inflammatory cytokines by inhibiting NF-κB activation. It also inhibits erastin-induced Ferro ptosis.

Eucalyptus extracts (Calyptol, Sanofi) has been the first product (and the most common product) used with warm-humid vaporization (WHV) in our studies aimed to control the COVID virus. Calyptol produced a complete and fast negativization of swabs in a significant number of subjects (this will be presented in a separate paper in preparation) and it is considered the 'model', safe virucidal product to be used for viral respiratory diseases and for COVID patients in warm-humid vaporization).

A new compound used for dry mouth (**Aldiamed Certmedica**) shows persisting effects in the mouth (up to 3 hours). Included in a jelly liquid are glycerin, sorbitol, xylitol, aloe, polyacrylate, xanthan gum; also, lactoferrin is parts of this product.

This registry study evaluated in a simple, low-cost in vivo model the effects of these 'virucidals' on the local presence in the mouth 'incubator' (saliva) of the COVID virus. As indicated, these subjects are asymptomatic or with very minor, transient symptoms (sore throat, infrequent cough and mild fatigue) with a positive swab. A 'virucidal' mouth medication /wash or inhalation had been suggested – 3-4 times, daily - to relieve the minor symptoms. After an initial swab (day zero) the tests were repeated after 3 days.

Results

Tolerability was very good. No side effects were observed. Table 1 and Figure 1-2 shows the decrease in positivity in the swab samples and the percent of positive cases at 3 days. The use of 'virucidals' resulted in a significant level of complete disappearance of positivity in most subjects at 3 days. The test was considered only as positive or negative without quantification of the level of positivity. All these virucidals resulted effective. The pharmaceutical form used in this experience seems to be important to assure persisting traces of the virucidal in the mouth. PhytoRelief with its composition produces the longest action (>3 hours) due to its slower release and persistence on the mucosal surfaces. These observations indicate a significant effect of virucidals on the viral contamination of the mouth with a relatively simple, cost-effective model. The lower presence of a virus charge or its decrease may significantly reduce contagiousness of most of these patients and the spread of viral material.

Prevention of external spread. The effects on the evolution of COVID-19 on single patients is, at the moment, unpredictable with this model but virucidals may assume a significant community value in preventing and controlling spreading. Lower viral charge may mean a lower level of dissemination.

Prevention of inner spread. It is also possible to consider that from the saliva (with its high viral content) while the mouth is acting as a viral growing chamber, the viral particles may be aerosolized into the lungs. The containment of viral growth in the mouth may also halt the spreading of the virus from the mouth to the trachea and into the bronchial tree.

Discussion

Antiviral drugs are the key drugs used for treating viral infections. Most antivirals target specific viruses; however, some broad-spectrum antivirals may be effective against a wide range of viruses. Antivirals do not directly destroy their target virus but, generally, inhibit their development. At the moment – studies are in progress - there are no specific antivirals, strongly active against the Wuhan viruses. Virucidals or viricides are not used as systemic drugs but deactivate or destroy many viruses inside or outside the body and specifically in 'border' anatomical areas (mouth, nose) when it is possible to apply them without causing damages or side effects.

Some of the most common virucidals are produced from natural plant extracts (pomegranate, eucalyptus and Australian tea tree oil, licorice, Baicalin) [4-13]. Eucalyptus extracts (as Calyptol, Sanofi) has been the first product (and the most common product) used with WHV in our studies aimed to control the COVID virus. Calyptol produced a complete and fast temporary negativization of swabs and it is considered the 'model', safe inhalatory virucidal to be used for viral respiratory diseases. It is also possibly effective even for symptomatic COVID patients in warm-humid vaporization.

Virucidals have been neglected: they are cheap, generally not protected by patents and basically have an adjuvant role in a low-cost market. The real target is to kill the COVID virus without side effects. Killing the virus early, in a preventive phase, could be the best option. Advanced disease, with all its clinical complications, appears difficult to manage. We have to deal, probably, with this COVID problem for a long time in prediction models [14-18]. The use of sequential antivirals at low-dose as a prevention may be more effective, safer and cheaper that the use of one antiviral. The combination of virucidals to block the viral spread and low-dose antivirals with other treatments may be possible solutions to control viral spread [19].

Respiratory viruses (including COVID-19) accumulate and grows in saliva and salivary glands in many patients; these situations are very difficult to eradicate. The presence of viruses in the salivary glands may induce a longer period of contagiousness and may be associated to super spreading with individuals infecting for a long

period of time a large number of individuals. In case of swelling, mild pain at the salivary glands, in otherwise asymptomatics a swab after massaging the salivary glands may be needed. Virucidals, used more often, early and aggressively, may help in decrease contagiousness. Mouth-derived viral diffusion in asymptomatic patients is very high risk. The role of oral mucosa in COVID-19 infection and salivary glands in the epidemic process of asymptomatic infections is documented [19]. ACE2, the important receptor for COVID-19, is very common in salivary gland epithelial cells; these cells have a high expression of ACE2 and can be easily infected.

The expression of ACE2 in salivary glands is higher than in lungs; this suggests that salivary glands are a potential target for COVID-19 and act as an incubator. SARS-CoV RNA is detected in saliva (the first incubator) before lung lesions. This partially explains the presence of asymptomatic infections and spreaders. For SARS-CoV, the salivary glands are, possibly, a major and neglected source of viruses migrating into saliva. The positive rate of COVID-19 in patients' saliva can reach 91.7%, and saliva samples are also be used to cultivate the live virus. COVID-19 may be transmitted by subjects with asymptomatic infections that originate, very often, from infected saliva. Most, persisting symptomatic infection (associated to super spreading) might be from salivary glands. Virucidals (Table 2) act where the virus is incubated (the incubators) and may have a very high community and management value, to be studied in large studies. In conclusion, virucidals may neutralize the virus in its primary incubators (mouth, saliva, salivary glands) and reduce the possibility of contamination.

Table 1: Results of the Use of Virucidals at 3 Days.

	PHYTO RELIEF CC	BENZYDR	BAICALIN	CALYPTOL	ALDIAMED
INCLUSION	11	8	6	10	4
3 DAYS	1	3	1	1	1
% OF POSITIVES	9,09	37,5	16,66	10	25

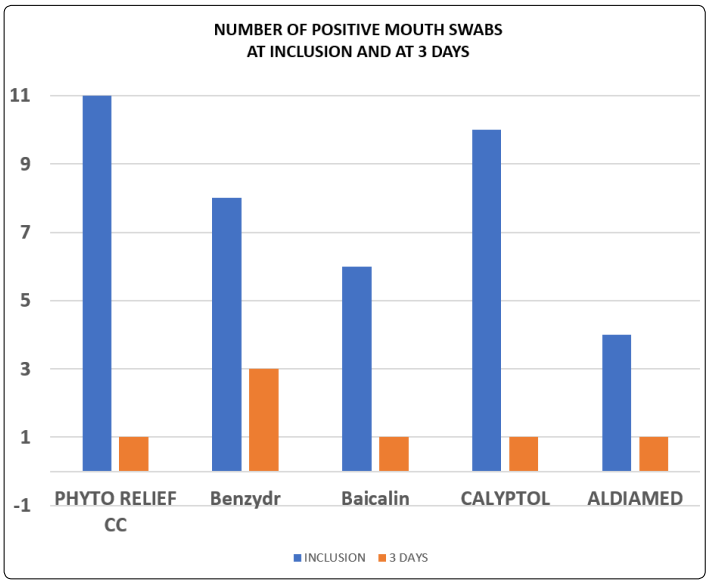

Figure 1: The decrease in positivity in the swab samples. The use of 'virucidals' resulted in a significant level of complete disappearance of positivity in most subjects. All virucidals were effective. Phyto-relief produced the longest virucidal action due to a slower release of its components. These results indicate an effect of virucidals on the viral contamination of the mouth/saliva. The lower presence of a virus charge or its decrease may significantly reduce viral spread from most of these patients.

Table 2: Some virucidals (some are shown in the list that may be very large) deactivate or destroy viruses. Most virucidals are used on surfaces and may be used as cleaning agents to stop the spread of COVID-19. Some virucidals may be used to control the proliferation of viruses in human surfaces and in 'viral incubators' (i.e., mouth).

Isopropyl alcohol, ethanol, n-propanol
Cyanovirin-N
EP 0978289 A1 with iodine
Griffithsin
Interferon
Lysol
NVC-422
Scytovirin
Urumin
Zonrox
Vecoy nanomedicines
Liposomes with virucidals
Calyptol
Australian tea tree oil
Benzydamine
Liquirice
Pomagranate

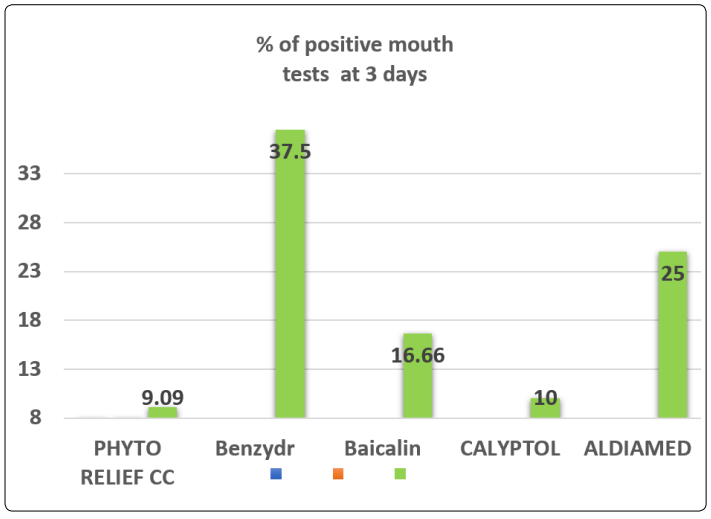

Figure 2: % of positive mouth tests at 3 days after using the virucidal 4 times daily.

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