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ORIGINAL RESEARCH

In Vitro Bactericidal and Virucidal Efficacy of Povidone-Iodine Gargle/Mouthwash Against Respiratory and Oral Tract Pathogens

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ABSTRACT

Introduction: Recent virus epidemics and rising antibiotic resistance highlight the importance of hygiene measures to prevent and control outbreaks. We investigated the in vitro bactericidal and virucidal efficacy of povidone-iodine (PVP-I) 7% gargle/mouthwash at defined dilution against oral and respiratory tract pathogens.

Methods: PVP-I was tested against *Klebsiella pneumoniae* and *Streptococcus pneumoniae* according to bactericidal quantitative suspension test EN13727 and against severe acute respiratory syndrome and Middle East respiratory syndrome coronaviruses (SARS-CoV and MERS-CoV), rotavirus strain Wa and influenza virus A

subtype H1N1 according to virucidal quantitative suspension test EN14476. PVP-I 7% gargle/mouthwash was diluted 1:30 with water to a concentration of 0.23% (the recommended concentration for "real-life" use in Japan) and tested at room temperature under clean conditions [0.3 g/l bovine serum albumin (BSA), viruses only] and dirty conditions (3.0 g/l BSA + 3.0 ml/l erythrocytes) as an interfering substance for defined contact times (minimum 15 s). Rotavirus was tested without protein load. A ≥ 5 $\log_{10}$ (99.999%) decrease of bacteria and ≥ 4 $\log_{10}$ (99.99%) reduction in viral titre represented effective bactericidal and virucidal activity, respectively, per European standards.

Results: PVP-I gargle/mouthwash diluted 1:30 (equivalent to a concentration of 0.23% PVP-I) showed effective bactericidal activity against *Klebsiella pneumoniae* and *Streptococcus pneumoniae* and rapidly inactivated SARS-CoV, MERS-CoV, influenza virus A (H1N1) and rotavirus after 15 s of exposure.

Conclusion: PVP-I 7% gargle/mouthwash showed rapid bactericidal activity and virucidal efficacy in vitro at a concentration of 0.23% PVP-I and may provide a protective oropharyngeal hygiene measure for individuals at high risk of exposure to oral and respiratory pathogens.

Funding: Mundipharma Research GmbH & Co. KG (MRG).

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INTRODUCTION

Antibiotic resistance is rising to dangerously high levels worldwide [1]. Oral and respiratory tract infections caused by bacteria such as *Streptococcus pneumoniae* and *Klebsiella pneumoniae* pose a particular threat because of the rise of antibiotic-resistant strains, with vulnerable patient populations at high risk of infection [2, 3]. Seasonal endemic viruses such as influenza are another significant cause of respiratory infection; worldwide, annual influenza epidemics are estimated to result in about 3–5 million cases of severe illness and about 250,000–500,000 deaths [4]. In addition to seasonal endemic viruses, emerging and re-emerging virus outbreaks such as severe acute respiratory syndrome and Middle East respiratory syndrome coronaviruses (SARS-CoV and MERS-CoV) require close contact for human-to-human transmission and can spread nosocomially [5, 6]. Unlike the remaining four coronaviruses, which are typically associated with mild, self-limiting respiratory illness, SARS-CoV and MERS-CoV cause severe respiratory symptoms and are associated with considerable mortality [7]. There is no vaccination or any specific antiviral treatment available for SARS-CoV and MERS-CoV. Outbreaks can, however, be quickly and effectively controlled with preventive strategies based upon early accurate viral diagnosis, knowledge of the current epidemiological season and effective hygiene practices to decrease the risk of transmission [8].

Effective hand hygiene minimises transmission of pathogens from contaminated hands of an infected individual through either direct person-to-person contact or indirectly via contamination of surfaces [9, 10]. Respiratory pathogens such as influenza are also transmitted via airborne dispersion of small particle aerosols ($\leq 5\ \mu m$) when an infected individual breathes, coughs or sneezes [11], while respiratory syncytial viruses, SARS-CoV and MERS-CoV can be spread by large droplets propelled through the air and inoculated into the eyes, nose and mouth at close range [12]. Considering these modes of transmission, oral hygiene by gargling, together with hand washing and mask use [13], may be beneficial to help minimise the risk of both community- and hospital-acquired respiratory infections. Gargling is also deemed to bring about favourable effects through removal of oral/pharyngeal protease that helps viral replication [14]. Effectiveness of the antiseptic agent in killing pathogens is paramount in selecting gargles/mouthwashes for protective hygiene and can be achieved by ensuring that antiseptic agents pass a standard bactericidal or virucidal activity test. A rapid action is also desirable, as the length of time that individuals are willing or able to keep the product in the oral cavity is limited.

Povidone-iodine (PVP-I) is a broad-spectrum antimicrobial that has been used in infection control and prevention for over 60 years [15] and is available in various preparations for use as a disinfectant for the skin, hands and mucosal surfaces, as well as for wound treatment and eye applications. PVP-I has well-established general antimicrobial activity, demonstrating in vitro efficacy against gram-positive, gram-negative and some spore-forming bacteria (clostridia, Bacillus spp.) and mycobacteria [16–20] and a wide range of enveloped and non-enveloped viruses [21–23]. Recent in vitro studies have demonstrated rapid virucidal activity of PVP-I products against Ebola virus, MERS-CoV and European reference enveloped virus [modified vaccinia virus Ankara (MVA)] [24, 25]. Considering the proven in vitro efficacy, gargling with PVP-I may be an effective method of preventing the spread of respiratory viruses when an individual is contaminated by the airborne/droplet route or after uptake via the mouth (such as when touching the mouth or food with contaminated hands). The benefit of gargling with PVP-I has already been noted in Japanese clinical respiratory guidelines [26].

This study investigated the in vitro bactericidal and virucidal efficacy of PVP-I 7% gargle/mouthwash against relevant oral and respiratory tract pathogens based on the European standards EN13727 [27] and EN14476 [28].

METHODS

Antiseptic product performance against test bacteria was performed according to bactericidal quantitative suspension test EN13727:2012 + A2:2015 [27] and against model viruses under defined test conditions, including temperature, contact time and interfering substances, according to virucidal quantitative suspension test EN14476:2013/FprA1:2015 [28]. Testing was performed from 11 February 2016 to 8 March 2016. This article does not contain any studies with human participants or animals performed by any of the authors.

Product Tested

The antiseptic product tested was 7% PVP-I gargle/mouthwash [brand-name Isodine, manufactured by Fukuchi Pharmaceutical Co., Ltd., Japan (bactericidal testing) and Mundipharma Pharmaceuticals Ltd. (virucidal testing)]. The 7% PVP-I solution was diluted with water (2 ml → 60 ml, equivalent to a concentration of 0.23% of the active ingredient) prior to testing, according to the manufacturer's instructions for use in Japan [29]. When using cell cultures in antiseptic product testing, the target cells are often more sensitive to the active ingredient. To overcome this, the test product was further tested at 1:10, 1:100 and 1:1000 dilutions of the 7% solution in bactericidal testing (corresponding to concentrations of 0.7%, 0.07% and 0.007% of PVP-I) and at 1:300 and 1:3000 dilutions in virucidal testing (corresponding to concentrations of 0.023% and 0.0023% of PVP-I).

Bactericidal Testing

Both gram-positive (*Streptococcus pneumoniae*, DSM 24048, ATCC 49619) and gram-negative (*Klebsiella pneumoniae*, DSM 16609) reference strains were tested.

Inactivation tests were conducted once in accordance with EN13727:2012 + A2:2015 [27] at $20.0 \pm 1.0\,°C$. A suspension of test organisms was added to the product test solution under dirty conditions [3.0 g/l bovine serum albumin (BSA) + 3.0 ml/l erythrocytes] as interfering substance. After the specified contact time (15 and 30 s), a 1-ml aliquot was taken, and the bactericidal activity in this portion was immediately neutralised with 3% Tween 80 + 0.1% histidine + 0.3% lecithin + 0.5% sodium thiosulphate. For each test suspension, two 1-ml samples were spread on at least two plates each. The number of surviving test organisms in the mixture was calculated for each sample and the reduction factor (RF) determined with respect to the corresponding test suspension. A reduction of bacteria of $\geq 5\log_{10}$ ($\geq 99.999\%$) compared with the control was considered to represent effective antibacterial efficacy according to European standards.

Virucidal Testing

The test viruses were coronaviruses SARS (strain Frankfurt) and MERS (HCoV-EMC/2012), influenza A virus (H1N1)pdm09 and non-enveloped human rotavirus strain Wa. The host cells used for the virus cultivation and suspension test were Vero E6 cells for SARS-CoV and MERS-CoV, Madin-Darby Canine Kidney (MDCK) cells for influenza virus A subtype H1N1 and MA104 cells for human rotavirus strain Wa.

Inactivation tests were conducted once in accordance with EN14476:2013/FprA1:2015 [28] at $20.0 \pm 1.0\,°C$. The virus suspension was added to the product test solution under clean (0.3 g/l BSA) and dirty conditions (3.0 g/l BSA + 3.0 ml/l erythrocytes) as interfering substance, except for the rotavirus suspension, which was tested without protein load (using distilled water as the interfering substance). The test assay comprised 100 μl virus suspension, 100 μl interfering substance and 800 μl PVP-I product (at the defined dilutions). A virus control mixture was also assessed using distilled water in place of the test product. After the specified contact time (15 s for SARS-CoV and MERS-CoV, 15 and 30 s for influenza, and 15, 30, 60 and 120 s for rotavirus), virucidal activity of the solution was immediately suppressed by dilution with nine volumes of ice-cold medium (MEM + 2.0% FCS) and serially diluted ten fold. Due to the immediate titration, no after-effect of the test product could occur. For each test

suspension, six wells (5 wells for SARS-CoV and MERS-CoV) of a microtitre plate containing a confluent monolayer of host cells were inoculated with $100\,\mu l$ of test suspension, and the cells were incubated at 37.0 °C in a humidified atmosphere under 5.0% CO_2.

After incubation, the medium was removed. For staining of influenza virus or rotavirus infectivity, cells were fixed for 10 min with ice-cold acetone/methanol (40:60) and then blocked with 1% BSA in phosphate-buffered saline (PBS) for 30 min and stained by the immunoperoxidase method. For testing against influenza A, a monoclonal antibody ($25\,\mu l$/well) (Chemicon, Temecula, CA) against influenza A (MAB8251) was applied. After incubation for 30 min at 37 °C, the plates were washed and incubated with secondary horseradish peroxidase-labelled anti-mouse antibody (anti-mouse-HRP, DakoCytomation, Germany) and finally with 3-amino-9-ethylcarbazole (AEC) substrate (Sigma, St. Louis, MO, USA). For testing against rotavirus, a peroxidase-labeled polyclonal goat antibody (BT81-2998-04, Biotrend, Köln, Germany) against human rotavirus was applied. After incubation for 30 min at 37 °C, the plates were washed and incubated with secondary horseradish peroxidase-labelled anti-goat antibody (Sigma-Aldrich, Germany) at a dilution of 1:500 and finally with AEC substrate. For all virus testing, AEC (dilution 1:500) was used to visualise antibody binding and infected cells were stained red. Stained cells were examined with a light microscope. The cells were examined microscopically for cytopathic effects (CPE). SARS or MERS infected cells were not stained, but examined microscopically for infectivity and cytopathic effects.

The virus titres were determined using the Spearman-Kärber method [30, 31] and expressed as tissue culture infectious dose 50% ($TCID_{50}$/ml). The virucidal activity was determined by the difference of the logarithmic titre of the virus control minus the logarithmic titre of the test virus ($\Delta\,\log_{10}\,TCID_{50}$/ml). This difference was given as an RF including its 95% confidence interval. A reduction in virus titre of $\geq 4\,\log_{10}$ (corresponding to an inactivation of $\geq 99.99\%$) was regarded as evidence of sufficient virucidal activity. The calculation was performed according to EN14476 [28].

RESULTS

Bactericidal Activity

The $\log_{10}$ reduction factors produced by PVP-I 7% gargle/mouthwash at defined dilutions against *Klebsiella pneumoniae* and *Streptococcus pneumoniae* under dirty conditions are shown by contact time in Table 1. Bacterial counts in the control samples were 7.61 $\log_{10}$/ml for *Klebsiella pneumoniae* and 7.34 $\log_{10}$/ml for *Streptococcus pneumoniae*. All bacterial counts were reduced by between > 5.20 and > 5.47 $\log_{10}$/ml (corresponding to a reduction in bacterial count of $\geq 99.999\%$) after 15 s of contact time at PVP-I concentrations of 0.7% (1:10 dilution) and 0.23% (1:30, i.e., recommended dilution). The lower concentrations of 0.07% and 0.007% did not reach the threshold reduction, except for the 0.07% solution against *Streptococcus pneumoniae* after 30 s.

Virucidal Activity

The $\log_{10}$ reduction factors produced by PVP-I 7% gargle/mouthwash at defined dilutions against each test virus are shown by interfering substance and contact time in Table 2. The viral titres present in the control samples under clean and dirty conditions, respectively, were 7.10 and 6.90 $\log_{10}$ $TCID_{50}$/ml for SARS-CoV, 6.90 and 7.10 $\log_{10}$ $TCID_{50}$/ml for MERS-CoV, 7.17 and 7.50 $\log_{10}$ $TCID_{50}$/ml for influenza virus A subtype H1N1 and 6.17 $\log_{10}$ $TCID_{50}$/ml for rotavirus (under clean conditions). All viral titres were reduced by between 4.40 and 6.00 $\log_{10}$ $TCID_{50}$/ml (corresponding to a reduction in viral titre of $\geq 99.99\%$ for all viruses tested) after 15 s of contact time with PVP-I gargle at a concentration of 0.23% (1:30, i.e., recommended dilution). The lower PVP-I concentrations of 0.023% (1:300 dilution) and 0.0023% (1:3000 dilution) that were tested against rotavirus and influenza did not reach a $\log_{10}$ reduction in viral titre ≥ 4, except for the 0.023% concentration against influenza under clean conditions.

Table 1 Bactericidal activity of povidone-iodine 7% oral solution against gram-positive and -negative bacteria under dirty conditions

Bacteria	Povidone-iodine concentration (%)	Log$_{10}$ reduction factor	
		15 s	30 s
Klebsiella pneumoniae	0.7	**> 5.47**	**> 5.47**
	0.23	**5.35**	**> 5.47**
	0.07	< 2.79	3.24
	0.007	< 2.79	< 2.79
Streptococcus pneumoniae	0.7	**> 5.20**	**> 5.20**
	0.23	**> 5.20**	**> 5.20**
	0.07	4.86	**> 5.20**
	0.007	< 2.52	< 2.52

Results shown in bold indicate bactericidal activity (≥ 5 log$_{10}$ reduction factor compared with control)
Dirty conditions: 3.0 g/l bovine serum albumin + 3.0 ml/l erythrocytes

DISCUSSION

Oral and respiratory tract pathogens represent a significant threat to human health. Nosocomial infections are widespread, especially among more vulnerable patients, and are important contributors to morbidity and mortality. A growing number of bacterial infections are becoming harder, and sometimes impossible, to treat as antibiotics become less effective, and vaccination against respiratory viruses either does not exist or has incomplete coverage. When there is an emerging infectious disease outbreak, practicing appropriate hygiene is recommended for both healthcare workers and individuals to limit the spread of infection by breaking the transmission. Oral hygiene could further improve the success rate of hygiene measures, especially against respiratory pathogens.

The data from this in vitro study demonstrated rapid bactericidal and virucidal activity of PVP-I gargle/mouthwash against all respiratory pathogens tested according to European standard requirements. The minimum 15-s contact time proved to be sufficient for PVP-I 7% gargle/mouthwash to be effective at the recommended dilution in Japan of 1:30 (equivalent to a concentration of 0.23% of the active ingredient). PVP-I solution has shown similar rapid antimicrobial activity in previous in vitro studies. Against bacteria, Shimizu et al. demonstrated complete efficacy of PVP-I 0.2% solution against clinical isolates of *Klebsiella pneumoniae*, *Serratia marcescens*, *Pseudomonas aeruginosa*, *Alcaligenes faecalis* and *Alcaligenes xylosoxydans* within 30 s using a simple methodology (the broth turbidity method) [18]. In another study, low concentrations of PVP-I gargle/mouthwash (0.23–0.47%) killed methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa*, including multidrug-resistant strains, within 15-60 s in the presence of oral organic matter from healthy volunteers, while 0.02% benzethonium chloride (BEC) and 0.002% chlorhexidine gluconate (CHG) were ineffective [32]. In a study comparing the bactericidal activities of three gargle/mouthwashes against isolate and standard strains of gram-positive (MRSA) and -negative bacteria (*Pseudomonas aeruginosa* and *Klebsiella pneumoniae*), PVP-I (diluted 15-, 30- and 60-fold) elicited rapid killing of all three strains after 30 s of exposure, while cetylpyridinium chloride (CPC) was effective only against gram-negative strains after 60 s of exposure, and CHG was ineffective [33].

In previous virucidal studies, PVP-I gargle was found to inactivate a panel of viruses

Table 2 Virucidal activity of povidone-iodine 7% oral solution against SARS-CoV, MERS-CoV, influenza virus A subtype H1N1 and rotavirus

Virus	Povidone-iodine concentration (%)	$\log_{10}$ reduction factor with 95% confidence interval						
		Clean conditions[a]				Dirty conditions[b]		
		15 s	30 s	60 s	120 s	15 s	30 s	
Influenza virus A subtype H1N1	0.23	**5.67 ± 0.43**	**5.67 ± 0.42**	n.d.	n.d.	**6.00 ± 0.47**	**6.00 ± 0.47**	
	0.023	**4.50 ± 0.54**	**4.83 ± 0.68**	n.d.	n.d.	0.33 ± 0.63	0.50 ± 0.65	
	0.0023	0.83 ± 0.54	1.00 ± 0.70	n.d.	n.d.	0.17 ± 0.58	0.17 ± 0.58	
SARS-CoV	0.23	**4.60 ± 0.80**	n.d.	n.d.	n.d.	**4.40 ± 0.79**	n.d.	
MERS-CoV	0.23	**4.40 ± 0.79**	n.d.	n.d.	n.d.	**4.40 ± 0.87**	n.d.	
Non-enveloped human rotavirus strain Wa	0.23	**≥ 4.67 ± 0.42**	**≥ 4.67 ± 0.42**	**≥ 4.67 ± 0.42**	**≥ 4.67 ± 0.42**	n.d.	n.d.	
	0.023	1.83 ± 0.54	2.00 ± 0.60	2.00 ± 0.60	2.17 ± 0.61	n.d.	n.d.	
	0.0023	− 0.33 ± 0.42	0.00 ± 0.60	0.17 ± 0.61	0.67 ± 0.42	n.d.	n.d.	

Results shown in bold indicate virucidal activity (≥ 4 $\log_{10}$ reduction in viral titre compared with control)

BSA bovine serum albumin, *MERS-CoV* Middle East respiratory syndrome coronavirus, *n.d.* not done, *SARS-CoV* severe acute respiratory syndrome coronavirus

[a] Clean conditions: 0.3 g/l BSA as interfering substance, except for rotavirus testing, which used distilled water

[b] Dirty conditions: 3.0 g/l BSA + 3.0 ml/l erythrocytes as interfering substance

including adenovirus, mumps, rotavirus, poliovirus (types 1 and 3), coxsackie virus, rhinovirus, herpes simplex virus, rubella, measles, influenza and human immunodeficiency virus, while CHG, benzalkonium chloride (BAC), BEC and alkyldiaminoethyl-glycine hydrochloride (AEG) gargles were ineffective against adenovirus, poliovirus and rhinovirus [22]. Eggers et al. demonstrated the virucidal activity of PVP-I 4% skin cleanser, 7.5% surgical scrub, 10% solution and 3.2% PVP-I/alcohol solution against Ebola virus and MVA and of PVP-I 7.5% surgical scrub, 4% skin cleanser and 1% gargle/mouthwash against MERS-CoV and MVA within 15 s of application [24, 25]. Application of PVP-I products with concentrations of 0.23–1% for 1–2 min reduced SARS-CoV virus infectivity from 1.17×10^6 $TCID_{50}$/ml to below detectable levels in a study by Kariwa et al., although shorter contact times were not investigated [23]. Ito et al. reported a reduction in viral infectious titres of avian influenza A viruses (H5N1, H5N3, H7N7 and H9N2) to below detectable limits by incubation for only 10 s with six different PVP-I products including 0.23% gargle and 0.23% throat spray [34]. The anti-influenza activity of PVP-I involves inhibition of viral haemagglutinin binding activity and viral neuraminidase catalytic hydrolysis [35]. In the present study, PVP-I oral solution at a concentration of 0.23% was also effective against non-enveloped rotavirus without interfering substance after 15 s of exposure, which is in contrast to in vitro work by Steinmann et al. [36], in which 7.5% PVP-I handwash was not active against the non-enveloped viruses tested, and by Sauerbrei and Wutzler [37], in which PVP-I took 5 min to inactivate polyomavirus SV40 and adenovirus.

In this study, the virucidal and bactericidal activity of PVP-I gargle/mouthwash was evaluated within a short exposure time (15 s) to reflect a similar or shorter time than the actual gargling time in real-life conditions, since the length of time that individuals are willing to keep an antiseptic product in the oral cavity is limited. PVP-I oral solution at a concentration of 0.23% was effective against all pathogens tested in this study after the minimum contact time of 15 s, regardless of protein load (except rotavirus, which was tested without protein load). Pathogens are eradicated by the active moiety (non PVP-bound 'free' iodine) being released into solution from the PVP-I complex, penetrating the cell wall and inactivating cells by forming complexes with amino acids and unsaturated fatty acids, resulting in impaired protein synthesis and alteration of cell membranes [38]. This basic mechanism of action leads to strong microbicidal activity expressed by multiple modes of action that include the disruption of microbial metabolic pathways, as well as destabilisation of the structural components of cell membranes, causing irreversible damage to the pathogen [39].

The results of this study suggest that the use of PVP-I gargle/mouthwash may be a useful protective measure against oral and respiratory tract infections. Indeed, following the H1N1 swine flu outbreak in 2009, Japan's Ministry of Health, Labour and Welfare recommended daily gargling as a protective hygiene measure to prevent upper respiratory tract infections (URTIs) [40], a practice supported by findings from studies that examined the role of gargling in both healthy individuals and those with frequent or persistent URTIs [14, 41, 42]. Limited clinical studies have been performed that used PVP-I gargle/mouthwash to reduce the incidence of respiratory infections in different settings. Shiraishi and Nakagawa showed a mean reduction rate in bacterial count immediately after gargling of 99.4% for PVP-I in volunteers (compared with 59.7% for CHG and 97.0% for CPC) and a significantly lower absence rate due to URTIs at a Japanese middle school where the use of PVP-I gargle was encouraged compared with schools where PVP-I gargle was not used [33]. In patients with chronic respiratory diseases, gargling with PVP-I was found to reduce the episodes of infections with *Pseudomonas aeruginosa*, *Staphylococcus aureus* (including MRSA) and *Haemophilus influenzae* by half [41]. Studies of prophylactic use of PVP-I gargle in patients requiring intubation have also shown significant reductions in oropharyngeal bacterial counts [43]. Oral hygiene using PVP-I may be of particular benefit in certain patient groups such as immunocompromised patients at risk of prolonged virus shedding (which can increase the potential for

resistance to antiviral drugs and for nosocomial transmission), patients with influenza to reduce the risk of secondary bacterial infection (that may appear, e.g., as otitis media in children and thus avoid the need for antibiotics) and possibly in hospitalised patients to prevent the spread of influenza during high season.

The safety profile of PVP-I is well established. In contrast to other antiseptic agents, PVP-I oral care products do not lead to any irritation or damage of the oral mucosa, even with prolonged use [44, 45]. Although measurable systemic iodine absorption may occur with the long-term use of PVP-I, its clinical manifestation as thyroid dysfunction is not very common [39].

A limitation of this work is that the clinical relevance of such in vitro test results remains unclear and needs to be supported by further investigations to evaluate the impact of gargling with PVP-I in real-life and clinical settings, although for ethical reasons, clinical studies involving highly infective and dangerous pathogens may not be feasible. Furthermore, our testing was limited to a few key respiratory microorganisms. We selected *Streptococcus pneumoniae* as the main cause of community-acquired pneumonia and meningitis and *Klebsiella pneumoniae* because, although not a common cause of respiratory tract infections, it is an emerging cause of multidrug-resistant nosocomial infection. In addition, these species represent both gram-positive and -negative bacteria. Although our study did not include other common bacterial pathogens causing pneumonia such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Haemophilus influenzae* and *Acinetobacter baumannii*, the efficacy of PVP-I against these pathogens has already been demonstrated in previous studies [16, 18, 32, 33, 41, 46].

CONCLUSION

In conclusion, our study results, taken together with (1) recommendations for gargling with antiseptic mouthwash for the control of oral and respiratory tract infections, (2) the rapid bactericidal and virucidal efficacy of povidone-iodine, including PVP-I gargle/mouthwash, against pathogens causing oral and respiratory

tract infections observed in other in vitro and in vivo studies and (3) the established safety profile of PVP-I from over 60 years of use, provide a strong rationale for the use of PVP-I oral solution for protective oropharyngeal hygiene management for individuals at high risk of exposure to oral and respiratory pathogens.

ACKNOWLEDGEMENTS

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