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REVIEW ARTICLE

The Critical Role of Personal Care Formulations in Infection Control: Sustaining Preventive Hygiene Practices for COVID-19 and Future Outbreaks

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ABSTRACT
The emergence and spread of a novel coronavirus designated as SARS-CoV-2 in late 2019 undeniably precipitated the greatest public health disaster of this new millennium. In absence of an available vaccine or virus-specific anti-viral drug, global health authorities issued several public advisories at the beginning of the pandemic and recommended mitigation measures based on the accumulating evidence and growing knowledge of the spread of this respiratory virus largely through airborne droplets and fomites. The recommended measures emphasized practicing respiratory, hand, and surface hygiene to break the chain of infection and reduce transmission of the virus. As a result of these recommendations, consumer products such as soap bars, liquid cleansers, alcohol-based hand sanitizers, oral rinses, and surface cleaners, in addition to masks (surgical, N95, etc) became the most sought-after commodities in markets across the globe. Beyond the public health recommendations, it was incumbent upon the manufacturers of such consumer products to substantiate their product efficacy against the SARS-CoV-2 virus, and later variants as they emerged, to ensure that the public confidence in the effectiveness of these products was not misplaced. In this article we will review the standard test methodologies and their scientific robustness to determine virucidal efficacy, as well as their relevance to consumer usage; discuss the contributory ingredients in each class of personal care formulations and their mechanisms of virucidal action; and establish the importance of the fully formulated products to ensure they are efficacious under consumer habit-oriented usage. Additionally, we will highlight the impact of hand, body, and oral hygiene practices and compliance in infection control for COVID-19 and their relevance for future outbreaks. Last but not the least, we will provide an overview of the existing regulatory challenges for claiming virucidal benefits from personal care formulations and propose ways in which opportunities to disclose proven benefits of these formulations would be beneficial to the public at large in sustaining efforts towards personal hygiene practices for infection prevention.

1. INTRODUCTION

The impact of COVID-19 on global public health and economies has been profound [1]. As of 11th July 2022, there were approximately half a billion confirmed cases and 6.3 million deaths reported to the World Health Organization (WHO COVID-19 dashboard). For about 12 months after the onset of the pandemic, there was no virus-specific vaccine or treatment to control or treat SARS-CoV-2 infection. Although since then more than 12 billion vaccine doses have been administered worldwide (estimate as of 2nd July, 2022), global inequity in vaccine distribution and availability is still a significant concern [2]. While an array of vaccines has proved to be safe and effective in saving lives, they do not confer 100% protection and additionally there are reasonable doubts surrounding their efficacy against future variants of SARS-CoV-2 [3,4]. Consequently, it is still critical to slow down the spread of infection by the circulating and emerging variants of SARS-CoV-2 through a range of non-pharmaceutical public health interventions (NPHIs) including personal hygiene measures. Until herd immunity to SARS-CoV-2 is achieved globally NPHIs are likely to remain as the first choice of preventive measures, particularly in places with low vaccine uptake and/or high vaccine hesitancy [5].

SARS-CoV-2 is transmitted chiefly through infectious respiratory fluid [6] and it has been recently reported that hand hygiene together with other protective measures such as wearing masks and physical distancing are associated with reductions in the incidence of COVID-19 [7]. Additionally, these measures have further contributed to the decrease in other respiratory infections during the pandemic [8]. Hand sanitation by washing with soap and water or with alcohol-based hand sanitizers is a simple primary preventive measure that people of almost all age groups can do independently. Unfortunately, this simple practice of handwashing that can substantially reduce transmission of germs remains an area of concern even within healthcare systems and services.

Concurrently, the oral cavity has come under increased scrutiny as it serves as an important portal for both ingress and egress of SARS-CoV-2. Since the discovery of high levels of ACE2 receptor expression in the oral cavity (chiefly the tongue and the oral mucosa) along with the presence of furin proteases that facilitate SARS-CoV-2 entry into cells, it has been firmly established that the oral cavity serves as a site for viral replication and propagation [9]. Consequently, saliva, which is a mixture of salivary secretions, pharyngeal secretions, and gingival crevicular fluid, has been shown to contain a significantly high titre of infective virus [10,11]. It is therefore reasonable to argue that oral health management through use of oral rinses (mouthwashes) with proven virucidal efficacy may play a significant role against transmission via salivary aerosols [12] and against disease progression by reducing viral load in the oral cavity [13]. Unfortunately, awareness towards this end is lacking among the public and focus needs to shift from dental health practitioner to a community-based setting [14].

While COVID-19 has undoubtedly reinforced hygiene compliance among the public and health care workers, numerous studies on preventive health behaviour during this pandemic and previous epidemics have clearly identified factors that influence adoption and sustenance of such behaviours. These include (i) perceived likelihood for infection, (ii) perceived severity if disease is contracted, (iii) perceived effectiveness of preventive behaviour, and (iv) perceived ability to perform the behaviour [15 16 17 18]. In this review, we are going to focus on a critical aspect of the perceived effectiveness of preventive behaviour with regards to the virucidal efficacy of marketed and widely available personal care formulations for hand/body and oral hygiene in reducing COVID-19 transmission. We will compare available standardized testing methodologies for virucidal efficacy determination, review the classes of ingredients present in the commercially available formulations, discuss how their broad-spectrum virucidal mode of action will continue to offer benefit across the evolving spectrum of SARS-CoV-2 variants, and finally suggest how country-specific regulatory authorities can play a direct role in communicating and amplifying the impact of these affordable and accessible hygiene formulations in reducing transmission of SARS-CoV-2.

2. EFFICACY DETERMINATION FOR CONSUMER PRODUCTS

In December 2015, a panel of scientists and public health experts was convened by the WHO to identify top emerging pathogens likely to cause severe outbreaks in near future and for which nil or insufficient preventive and curative solutions exist. Seven pathogens requiring urgent R&D efforts were shortlisted in this workshop (https://cdn.who.int/media/docs/default-source/blue-print/2015-workshop-on-prioritization-of-pathogens.pdf?sfvrsn=50b6ddaa_2). Intriguingly, the list included highly pathogenic coronaviruses, a prediction which has now been validated by the emergence of SARS-CoV-2. Presently, market-driven pharmaceutical R&D models do not allow for investment in new or improved interventions for diseases that are sporadic or unpredictable, especially when they occur in countries with low investment in health infrastructure and delivery. The challenge becomes significantly greater when faced with a novel disease with pandemic potential such as COVID-19. Interestingly, almost all the emerging / re-emerging pathogens captured in the WHO list are of zoonotic origin and belong to the family of large, enveloped viruses with single-stranded RNA genome. This raises a pertinent consideration centred on the probable commonality of modes of transmission and transmissibility of these pathogens, their survival on various surfaces, and most importantly their infectivity. Can we find a blueprint for formulating widely accessible and affordable commercial non-pharmaceutical hygiene-centric interventions that can achieve broad-spectrum inactivation of these emerging / re-emerging pathogens and serve as the first line of defense against these viruses? The modes of inactivation for these formulations will ideally be based on disrupting the shared physico-chemical attributes of these viruses like human host-derived lipid bilayer, virus-derived envelope proteins, and the RNA genome. Towards this end, we have reviewed in the following sections standard methodologies employed for proving virucidal efficacy of commercial formulations, the classes of actives present in marketed hygiene products and their modes of virucidal action, the criticality of personal hygiene for the wider benefit of public health and well-being, and last but not the least the importance of reporting virucidal efficacy of a fully formulated product as available in the market versus a minimum viable prototype or a neat active composition.

2A. METHODOLOGIES FOR PROOF OF EFFICACY

For assessing the antiviral efficacy of products, two widely used methods in the industry are ASTM International standard E1052-20 (https://www.astm.org/e1052-20.html) and European Committee for Standardization (CEN) standard 14476:2013+A2:2019 (https://infostore.saiglobal.com/en-us/Standards/BS-EN-14476-2013-A2-2019-238423_SAIG_BSI_BSI_2753744/). These standards have been developed by technical experts from industry, academia, and other interested organizations using an open and transparent consensus process. Fundamentally, both methods are based on the same suspension test principle: virus/soil (interfering substance) added to a suspension of product for a desired contact time, after which the sample is neutralized, diluted, and added to the cell culture. Appropriate controls, including virus recovery, neutralizer effectiveness (suppression of product efficacy), cytotoxicity and cell culture viability, are described in both standards. Host cells are incubated and examined microscopically for virus-specific cytopathic effects and product-specific cytotoxic effects.

Results from the suspension tests are reported as either plaque forming units per mL (PFU/mL) or the 50% tissue culture infective dose per mL ($TCID_{50}$/mL) as determined using the Spearman-Karber method [19]. In situations where a sample contains no detectable virus, a statistical analysis is performed based on the Poisson distribution (https://www.fda.gov/media/71394/download) to determine the theoretical maximum possible titer for that sample. The average $\log_{10}$ reduction is calculated as the difference in PFU/mL or $TCID_{50}$/mL between the test product and virus recovery control. Testing of products against SARS-CoV-2 and its variants requires facilities that are designed and equipped for work with infectious agents at the correct Containment level or Biosafety level.

In the suspension-based viral assays, consumer products typically are evaluated under relevant use conditions; liquid hand and body washes are assessed at a 50% dilution and hand rubs/sanitizers/mouth rinses are tested neat at a temperature of 20°C. In the case of bar cleansing products, an 8% dilution is evaluated at a higher temperature to prevent gelling which would significantly interfere with conduct of the assay. The contact time between the virus and product in the suspension assay should reflect the intended usage of the product, i.e., how the consumer normally uses the product. The CDC recommends at least a 20-second scrubbing of hands with a cleanser, and for hand rubs, the product is rubbed over all surfaces of the hands and fingers until dry (~20 seconds) (https://www.cdc.gov/handwashing/when-how-handwashing.html).

Some products result in cytotoxicity at one or more dilutions that may impact the $\log_{10}$ reduction reported in the suspension assay. If cytotoxicity is present, a technique known as large volume plating can be employed to improve the detection of low levels of residual virus, thus increasing the $\log_{10}$ reduction observed. Where mandated reductions are required for product registration, large volume plating or other techniques may be necessary to demonstrate the desired reduction.

The EN14476 standard stipulates minimum test conditions for different antiseptic and disinfectant products. Deviations to the standard are required when other product forms, such as mouth rinses, are tested or when the defined limits cannot be implemented, as in the case of bar cleansers. The ASTM method allows for a variety of different product forms, including those not labelled as antiseptics or disinfectants, to be tested using the same general procedures. Not all the testing parameters are specified in ASTM E1052, and the user defines appropriate conditions based on relevance to the test product. For example, contact times are not stated, and the recommendation is to test products at times that are reflective of the intended use. Since both standards provide options/ranges, preparation of a protocol, where all details of the evaluation, including deviations and justifications, are documented, is common practice.

The EN14476 method specifies a pass criterion of a 4-log_{10} reduction of the virus for antiseptics and disinfectants, while in the E1052 standard, it is the responsibility of the user to refer to the appropriate regulatory agency for performance standards of virucidal efficacy. In the European Union, the Biocidal Products Regulation (https://echa.europa.eu/documents/10162/23036412/bpr_guidance_assessment_evaluation_part_vol_ii_part_bc_en.pdf/950efefa-f2bf-0b4a-a3fd-41c86daae468) denotes use of the EN14476 standard for making antiviral claims for products registered as biocides. Health Canada regulations for human-use antiseptics (https://www.canada.ca/content/dam/hc-sc/documents/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/human-use-antiseptic-drugs/antiseptic_guide_ld-eng%20REPLACED%20October%202019.pdf) state the minimum log_{10} reduction required and allow either the ASTM International or CEN standard to be used. Products intended for normal consumer use, such as bar and liquid cleansers, may not be categorized as antiseptics, but by nature of their formulations, do show demonstrable antiviral efficacy ($\geq$99.9%) under consumer-relevant conditions.

2B. CLASSES OF INGREDIENTS AND THEIR VIRUCIDAL MODE OF ACTION AGAINST ENVELOPED VIRUSES

Commercially available personal care formulations relevant for risk mitigation in relation to SARS-CoV-2 transmission belong to the broad classes of hand hygiene and oral hygiene products. Hand hygiene products are available in a wide variety of formats namely soap bars, liquid hand and bodywashes, sanitizers (gel and spray) and wipes. Oral hygiene, on the other hand, is driven primarily by oral rinses or mouthwashes. As summarized in table 1, the widely different product formats contain an array of ingredients including surfactants, alcohol, quaternary ammonium compounds, as well as antiseptics like salts of chlorhexidine (CHX) and povidone-iodine. All the above-mentioned classes of ingredients in personal care formulations target enveloped viruses such as SARS-CoV-2 through singular or combinatorial extracellular modes of action wherein they disrupt the viral envelope via destabilization of the lipid bilayer, denature key proteins of the viral envelope (such as the spike protein of Coronaviruses) necessary for initiating infection, and degrade the nucleocapsid (including the RNA/DNA genome)[20,21]. Empirical data establishing the broad-spectrum virucidal efficacy of these ingredients have been extensively reviewed [22-25]. Although many studies follow the regulatory accepted standardized protocols for estimating virucidal efficacy, they occasionally suffer from the drawback of conducting the tests at lower dilutions and extended durations that are not relevant from end-user perspective. Ideally, suspension tests for bar soaps and liquid cleansers (hand and bodywashes) should be conducted at a range of 10 to 60 seconds contact duration at 8% and 50% dilution, respectively. On the other hand, application time for hand sanitizers typically range between 10 – 15 seconds in an undiluted form. Similarly, oral rinses are recommended to be used for 30 seconds without dilution. It is strongly recommended that manufacturers adhere to the above-mentioned guidelines when reporting efficacy of their products.

Through the first wave of the pandemic, published efficacy data for marketed personal care formulations were chiefly derived against the parental strain of SARS-CoV-2. However, legitimate concerns were raised within the public-at-large regarding the validity of this efficacy data against emerging variants of concern (VOCs) which demonstrated both enhanced transmissibility and ability to evade adaptive immune responses acquired from previous infection. Investigations by Meister and colleagues revealed similar inactivation profiles of two VOCs (namely Alpha and Beta) when compared to the parental strain, indicative of a comparable susceptibility towards surface disinfection [26]. Similarly, it was argued by Ijaz and colleagues that personal hygiene-based interventions for infection prevention and control should continue to be effective on account of the broad-spectrum virucidal mode of action of the ingredients [27]. This was conclusively demonstrated through an evidence-based approach by Mukherjee et al. [28] for hand hygiene and by Anderson et al. [29] for oral hygiene.

Table 1. Summary of ingredients present in different classes and formats of personal care formulations and their generic virucidal mode of action.

Personal care product	Class of Ingredient	Examples	Mode of virucidal action
Soap Bar	Surfactant	Na- and K- salts of short and long-chain fatty acids like laurate, oleate and palmitate	1. Physical removal of viral particles through rinsing 2. Disruption of lipid bilayer 3. Denaturation of viral proteins
Bodywash	Surfactant	Anionic (ALS, SLS, SLES) Non-ionic (Tween20)	
Liquid Handwash	Surfactant		
	Organic acids	Lactic acid, Citric acid, Salicylic acid, Benzoic acid	1. Disruption of lipid bilayer 2. Denaturation of viral proteins
Alcohol-based hand sanitizer (Gel, spray, wipes)	Alcohol	Ethanol Isopropanol	1. Disruption of lipid bilayer 2. Denaturation of viral proteins 3. Damage to the genome
Non-alcoholic hand sanitizer, Disinfectants (Gel, spray, wipes, liquid)	Quaternary ammonium compounds	Benzalkonium chloride, Didecyldimethylammonium chloride	Disruption of lipid bilayer
Mouthwash	Quaternary ammonium compounds	Cetylpyridinium chloride Chlorhexidine salts (gluconate, digluconate, acetate)	Disruption of lipid bilayer
	Antiseptic	Povidone-iodine	Disruption of proteins, fatty acids, nucleotides

2C. IMPORTANCE OF ASSESSING FULLY FORMULATED PRODUCTS

Bar soaps, liquid cleansers, and sanitizers for hand & body hygiene

Cleansers are a category of products that impart germ protection benefits during use. Frequent engagement in hand hygiene with use of products in this category finds an undisputable role in infection prevention efforts for known and emerging pathogens.

Surfactants for wash off products and alcohol for leave-on sanitizers form the base for such products with inclusion of actives, rheology builders and fragrance contributing to performance and sensorial. While virucidal and bactericidal properties may be understood at an ingredient level, for surfactants and actives, the choice and level of inclusion contributes to overall effectiveness of a final product.

As with efforts towards infection prevention through sanitation and disinfection in hospital settings, use of cleansers in community settings by general population should consider context and user frequency for delivering efficacy. Therefore, product design for cleansers should take into consideration relevance of in-use dilution, contact time with skin and types of microorganisms for hand hygiene. This makes a valid reason to test fully formulated cleansing products designed to address preventing the transfer of pathogenic load on skin with every use for the favourable public health outcome of infection prevention and control at community level.

Mouthwashes for oral hygiene

The antiviral performance of oral rinses is dependent on a combination of the active ingredients, their intrinsic efficacy against the infectious agent, and their bioavailability during and / or after use. In the context or oral rinses, the active ingredients in most wide use are dequalinium chloride, benzalkonium chloride, cetylpyridinium chloride (CPC) and chlorhexidine, which all belong to the broad class of hygiene actives collectively termed quaternary ammonium compounds. Numerous publications have investigated the performance of oral rinses against SARS-CoV-2 and have shown CPC to be reproducibly effective against the virus [30,31] and several variants [29] whilst data on the efficacy of chlorhexidine has been more varied [32]. Whilst such assessments provide vital insights into the efficacy of oral rinse products both in maintaining oral health and as interventions against disease transmission via aerosols there is an ongoing need to develop new methodologies which reflect disease transmission both in the laboratory and community setting.

3. IMPACT OF HAND, BODY AND ORAL HYGIENE PRACTICES ON PUBLIC HEALTH AND WELL-BEING

It is well established that general improvements in personal hygiene practices and public health infrastructure can reduce the burden of certain communicable infections. In an extensive study reviewing the causal link between hygiene and infections, Aiello and Larson concluded that there is substantial evidence linking appreciable reduction of infections (> 20%) after implementation or changes in hygiene measures or behaviours [33]. Good personal hygiene involves keeping all parts of the body clean and healthy through regular bathing, hand sanitation, oral rinsing, face cleansing, and intimate hygiene. In the following section, we are going to briefly discuss the tenets of personal hygiene, focussing on hand, body, and oral hygiene, as an effective countermeasure for the on-going pandemic and for future outbreaks.

Hand hygiene

Our hands play a vital role in transmission of infection in healthcare, industrial, community and domestic settings. It is estimated that eighty percent of common infections are spread by hands (https://www.cdc.gov/handwashing/why-handwashing.html). Regular handwashing and hand sanitation helps to remove germs, avoid getting sick, and prevent the spread of infectious diseases, including diarrhoeal diseases and respiratory diseases such as COVID-19. Good hand hygiene is a highly cost-effective public health measure, and a cornerstone of safe and effective health care. It is crucial to protecting against a range of endemic diseases, stopping the transmission of COVID-19, and preventing future outbreak-related diseases. It is also critical to combatting antimicrobial resistance (AMR). The 'Hand Hygiene For All' global initiative by the W.H.O. is designed around three stages: responding to the immediate pandemic, rebuilding infrastructure and services, and last but not the least, reimagining hand hygiene in society (https://www.who.int/initiatives/hand-hygiene-for-all-global-initiative). Handwashing with soap could protect about 1 out of every 3 young children who get sick with diarrhoea and almost 1 out of 5 young children with respiratory infections like pneumonia. The use of an alcohol-based hand sanitizer in U.S. classrooms reduced absenteeism due to infection by about 20% overall among 16 elementary schools and 6,000 students [34,35]. A study, with the objective of evaluating the effect of hand hygiene with a branded germ protection soap through a hygiene promotion programme showed a significant reduction in episodes of diarrhoea, acute respiratory infections, and eye infections with a favourable outcome of reduction in school absenteeism (by 27%) due to illness amongst children (aged approximately 5 years old)[36].

Table 2. Impact of hand hygiene and hand hygiene education in reducing incidences of communicable diseases.

Impact on	Key findings	Refences
Diarrhoeal infections	**23-40% reduction** in the number of people who get sick with diarrhoea	37 38 39 https://www.cdc.gov/handwashing/global-handwashing-day.html
	58% reduction in diarrheal illness in people with weakened immune systems	40 https://www.cdc.gov/handwashing/global-handwashing-day.html
Respiratory infections	**16-21% reduction** in the risk of respiratory illnesses, like colds, in the general population	41 38 https://www.cdc.gov/handwashing/global-handwashing-day.html
School absenteeism	**29–57% reduction** in absenteeism due to gastrointestinal illness in schoolchildren	42 https://www.cdc.gov/handwashing/wcms-inc/global_handwashing_day.html
Infections in health care setting	**up to 50% prevention in** avoidable infections acquired during health care delivery	https://www.who.int/teams/integrated-health-services/infection-prevention-control/hand-hygiene
On transmission and infections by multidrug resistant organisms in health-care settings with significant increase in HH compliance	Significant **reduction** in the annual overall prevalence of **HAI (42%)** and MRSA* **cross transmission rates (87%).**	43 https://cdn.who.int/media/docs/default-source/integrated-health-services-(ihs)/infection-prevention-and-control/mdro-literature-review.pdf?sfvrsn=88dd45c7_2
	51% decrease in hospital-acquired MRSA cases during the 12-month*	44 https://cdn.who.int/media/docs/default-source/integrated-health-services-(ihs)/infection-prevention-and-control/mdro-literature-review.pdf?sfvrsn=88dd45c7_2
	Significant reduction of MRSA rates from 0.52 to 0.24 episodes/1000 patient days	45 https://cdn.who.int/media/docs/default-source/integrated-health-services-(ihs)/infection-prevention-and-control/mdro-literature-review.pdf?sfvrsn=88dd45c7_2

* Statistics not reported

Body Hygiene:

Bathing is the main process of cleaning the body externally and is very important to ensure personal hygiene of body. Daily bathing with soap and water helps to prevent body odour and remove harmful microbes from the body [https://www.cdc.gov/handwashing/index.html]. Evidence confirming survival of SARS-CoV-2, its emerging VOCs and other viruses on a vast array of surfaces including skin for several hours and days presents new understanding of survivability of this novel virus. Human Angiotensin-converting enzyme 2 (ACE2) receptors act as primary attachment site for SARS-CoV-2. The evolving findings postulate that the presence of ACE2 in skin presents skin as a possible site for entry and transmission of SARS-CoV-2. A growing body of evidence on the role of skin as a site not limited to for entry and transmission, but also survival of SARS-CoV-2 for long hours on skin sets another area to be focused on for prevention [46,47]. As common habit centred regular personal hygiene practices, bathing in addition to hand washing with soap bars and liquid cleansers will play a pivotal role in prevention. The prevention mechanism will be by virucidal effects of products on skin's surface pathogens during the process of lathering and washing. Henceforth the use of cleansers will still stay relevant for other pathways like faecal-oral and skin contact. The role of regular personal hygiene habits should not be under-estimated as VOCs continue with re-infections characteristic of COVID-19[48].

Oral hygiene

The oral cavity presents a uniquely complex environment, combining a diverse and abundant microbiome with an array of surfaces including teeth, gums, mucous membranes, and the salivary milieu. Effective oral hygiene, including twice daily brushing with a fluoride toothpaste (https://www.fdiworlddental.org/promoting-dental-health-through-fluoride-toothpaste), is essential to good oral health and thus is integral to personal hygiene as well as overall health, well-being, and quality of life. Poor oral hygiene leads to plaque build-up, tooth decay, malodour (halitosis) and gum disease. The Global Burden of Disease Study 2019 estimated that oral hygiene issues affect close to 3.5 billion people worldwide (https://www.who.int/health-topics/oral-health#tab=tab_1) and individuals at risk of gingivitis are recommended to use a toothpaste with antimicrobial or antiplaque action potentially in combination with an effective mouthwash [49].

Whilst the connection between effective oral hygiene and good oral health is well recognised, the role of oral hygiene in relation to susceptibility to respiratory viral infections is being investigated widely [50,51]. The global pandemic has increased focus on the importance of the oral cavity and oral hygiene within the context of community transmission of viral diseases. Broadly, this importance can be grouped into three broad areas. Firstly, and most obviously, the oral cavity is the origin of the aerosols created through breathing and coughing [12,52,53]. Secondly saliva contains high levels of infective virus [10,54] compounding the importance of saliva and salivary aerosols in disease transmission[13] and potentially contributing to the reported importance of aerosols to differences in transmissibility between SARS-CoV-2 strains [55]. Thirdly the detection of ACE2 and TMPRSS2 receptors in the oral epithelia and the demonstration of viral infection of oral tissue in-vivo [56] which may contribute to salivary titre or potentially aggravating systemic infection via an oral-vasculo-pulmonary route [57] or via inflammatory stimulation [58]. It is therefore not surprising that employing logistic regression models adjusted for demographic, behavioural, and clinical factors, Marouf et al reported a strong association of periodontitis with COVID-19 complications. Similarly, in a study aimed at understanding the potential effect of oral health on COVID-19 illness severity in recovered patients, Kamel and colleagues found that oral health and COVID-19 severity showed a significant inverse correlation. Moreover, the correlation between oral health with recovery period and C-reactive protein (CRP) values (a marker for inflammation) also revealed a significant inverse correlation showing that poor oral health was correlated to increased values of CRP and delayed recovery period [59]. Insights such as these have highlighted the importance of good oral hygiene practice to maintain oral health, and the potential for mouthwashes with proven antiviral efficacy, such as those containing cetylpyridinium chloride (CPC) [29-32], which may help mitigate virus transmission.

To summarize, the role of hand and oral hygiene in infection prevention and control (IPAC) strategies would broadly remain the same for any known or unknown infection-causing microorganisms with potential for causing localized or global outbreaks. The opportunity provided by this pandemic to bring personal hygiene at the forefront of prevention efforts is invaluable from a public health perspective.

4. HAND HYGIENE COMPLIANCE DURING AND AFTER COVID

As the world returns to much anticipated 'normalcy', more relaxed individual attitudes to SARS-CoV-2 can be observed in terms of preventative behaviours [60-62]. Fuelled by removal of mask mandates by governments and greater attention shifting to vaccination drives, attitudes towards hand hygiene can be expected to decline when compliance in this space cannot be regulated in community settings. Hand hygiene occasions in general populations are varied, where use of products and engagement in behaviour are a matter of individual choice [63]. Use of soap and sanitizer for hand hygiene was a behaviour encouraged with messaging to drive frequency as well as the correct way of using product and cleaning during the pandemic. Twenty seconds or singing happy birthday twice became the prescriptive way to wash hands by the WHO where the same message was relayed in all corners of the world as instructions on how to wash (https://www.cdc.gov/handwashing/when-how-handwashing.html & https://www.who.int/docs/default-source/coronaviruse/who-hh-community-campaign-finalv3.pdf). The scale of preventative behaviours amplified during COVID-19 played a pivotal role in public adherence with acceptance and adherence with lesser hesitation and restrain.

The barriers for hand hygiene were overcome significantly during the first two years of the pandemic where education played a role in attitudes of reduced dissent towards hand hygiene and other preventive measures (https://www.who.int/publications/i/item/covid-19-global-risk-communication-and-community-engagement-strategy). COVID-19 pandemic has undoubtedly raised awareness and engagement in hand hygiene behaviours at a scale unthinkable if not for the unified and intensive promotion as a key measure of prevention [64]. A major contributory factor driving rapid adoption was due to the habit familiarity of washing hands with soap. This makes a case for the power of consistent and sustained messaging, coupled with product availability at a home setting and access to hand hygiene solutions and facilities when out of home.

Pandemic fatigue and messaging desensitization have been identified by the WHO with recommendations on messaging to sustain hygiene behaviours for protection from COVID-19 (https://www.who.int/publications/i/item/covid-19-global-risk-communication-and-community-engagement-strategy). Sensitization to health messaging leading to non-action has been reported in diverse fields [65,66]. The psychological aspects of driving non action by individuals even when implications are evident are complex. The role of soap and alcohol-based sanitizer for the protection against germs that can cause a life-threatening new infection gained a new level of understanding. Even with this level of knowledge, slipping back to pre-pandemic behaviours is a public health concern [67].

The joint report released by the WHO and UNICEF titled, “A global call to action to make hand hygiene a priority in policy and practice” in October 2021 thoroughly examined the problems and barriers that need to be addressed at a global scale. Governance, financing, capacity development, data and information, and innovation are identified as key accelerators to achieve hand hygiene for all (https://www.cdc.gov/handwashing/when-how-handwashing.html). Cohesive public-private approaches with multi-stakeholder consensus will be required to achieve the objective of quadrupling the current rate of progress to achieve the Sustainable Development Goal target on hand hygiene (https://www.who.int/publications/i/item/9789240036444). To translate intention to practice, availability of products becomes the last mile determinant to engage in hand hygiene. It is therefore imperative to offer products catering to various price points, sensorial and cleansing needs for individual or family relevance. Affordability to the majority and below average pricing, as done with Lifebuoy bar in India sold at INR 5.00 (US$ 0.07) is an example referenced in the WHO’s global call to action document on hand hygiene. Innovations in cleanser technologies to overcome barriers to hand hygiene based on real user problems like effects of frequent washing on skin, time taken for process, inconveniences related to product use and water shortage will be pertinent to trigger and sustain this life-saving habit. Innovations designed for enjoyability becomes a key driver for this mundane activity with no immediate tangible benefit as pathogens are invisible and action of removal not visually evident.

Education has a key role to play on simplifying and visualizing how pathogen transmission happens in daily lives, with modes of action of product and efficacy all building up to reason for soap use. Health messaging for COVID-19 contextualized the mechanics of how and when to wash or use hand sanitizer, making the occasions relatable at the onset [68]. Valuable insights on how trust in science leads to positive engagement in preventative behaviours during the pandemic can be used as learnings to refine messaging as continuity of reminding becomes a way to sustain this life-saving habit [69]. It becomes a joint responsibility of public-private entities to tackle socio-demographic disparities in knowledge, practices, and ability to comply with public health recommendations that encourages use of soap and hand sanitizers to curtail spread of pathogens.

5. OVERVIEW OF REGULATORY CHALLENGES IN EXISTING FRAMEWORK FOR CLAIMING VIRUCIDAL BENEFITS FROM PERSONAL CARE FORMULATIONS AND A PROPOSAL FOR DRIVING ENHANCED ADOPTION OF HYGIENE PRACTICES

Despite overwhelming evidence on how bar soaps and liquid cleansers help in breaking the chain of infection and significant efforts by global policy drivers to promote hand hygiene, positioning these personal care formulations for infection prevention becomes a paradox at a country level. The contradiction is rooted in two points of contention. Firstly, soaps and cleansing liquids used for daily hygiene requirements of washing hands and bathing are positioned under the cosmetic classification. Under this classification, communicating the mode of action of soap bars and cleansers on virucidal effects is not recognized. Although the mode of action of such products are in the realm of inactivating transient, surface pathogens and prevention of entry to body, the current regulations identify with prevention only to be a function of drug or biocidal product. Cosmetic products that are effective at removing pathogens do not necessarily contain active ingredients that are regulated as biocides. It becomes unviable to bring common daily use cleansers under the biocide or drug classifications that would require over engineering of products for general use and in some geographies, limit availability for purchase in general stores where these products are currently accessed.

The second area of concern for regulators is their own opinion on the comprehension factor amongst users when soaps and cleansers communicate role in efficacy against pathogens for infection prevention. While products can always be tested on a relevant strain for a particular infection simulating in use conditions, simplification of the science plays a big role in messaging and communications. For instance, while the general population would have high rate of awareness on COVID-19, seasonal flu or stomach infections, it cannot be expected that the strain names of SARS-CoV-2, Influenza A or Rotavirus will be comprehended. Therefore, using common parlance like COVID-19 coronavirus, Flu virus or stomach infection causing germs becomes more direct and relevant. Any messaging on product efficacy, action of washing away pathogens, and contextualizing the role of soap in terms of names of infections and transmission moments are helpful to drive behaviour change and encourage continuation of habit.

Given the mass scale and rapid knowledge dissemination on skin as a substrate for pathogen transfer and soap and cleansers as protection interventions with COVID-19, it is not expected that a common person would interpret benefits as curative. Henceforth, the concern around a misinterpretation by users of such products offering cure should no longer be considered valid. Industry and regulators have a duty to strive for a regulatory framework that offers both curative and preventative (vaccines) drug products as well as cosmetic products with a proven role in reducing risk of infection and transmission to be available to consumers, so they are able to construct a robust, high compliance, consumer hygiene regime.

To strengthen efforts between global-local health authorities and private entities on achieving infection prevention targets, fighting future outbreaks and pandemics, and reducing global burden of disease, it is pertinent for cosmetic regulations to revisit these barriers and work with industry on overcoming them for the greater benefit with required controls like availability of efficacy data, consumer comprehension data to substantiate non-misleading messaging and not adding to public panic but guiding towards right behaviours with trustworthy, engaging and responsible communication.

6.CONCLUSIONS

In a stirring article published in Lancet, Richard Horton has aptly summarized that "COVID-19 is not a pandemic. It is a syndemic"[70]. In the mid-1990s, an American medical anthropologist Merrill Singer and colleagues coined the term syndemic to define approaches that reveal biological and social interactions that are important for prognosis, treatment, and health policy. It can be argued in the same vein that the unprecedented character of COVID-19, which makes any comparison with recent health disasters almost irrelevant, needs a syndemic approach to make our future COVID-19 secure. The random nature of the initial shock in the first quarter of 2020 continues to define this global health crisis with a totality that has impacted almost every dimension of our society – health care, public hygiene, international mobility, social interactions, and many more. Despite the undoubtable success of multiple vaccines targeting SARS-CoV-2, a significantly high level of uncertainty continues unabated on account of both biological (emerging SARS-COV-2 VOCs) and socio-eco-political (inequity in vaccine distribution & availability) factors. Towards this end, affordable and widely available non-pharmaceutical interventions offer a framework and toolkit for infection prevention and control in future outbreak preparedness, readiness, and response at the community level. Regular soap bars, cleansing liquids (hand and bodywashes), alcohol-based sanitizers, and oral rinses used for daily hygiene present widely accessible and affordable interventions, especially those with proven virucidal effects under consumer relevant conditions of product dilution and duration of usage. Although virologist Christian Dorsten had famously remarked “there is no glory in prevention”, these personal care hygiene products based primarily on the broad-spectrum armamentarium of surfactants, alcohols, and quaternary ammonium compounds are and will continue to be effective in reducing transmission of SARS-CoV-2 and preventing its spread irrespective of the mutational profile of the circulating or emerging VOC. Adequate solutions should therefore be identified by the regulatory authorities for the role of first line of defence in reducing pathogen load for infection prevention, and to allow for such affordable and widely accessible product formats (such as soaps bars, liquid bodywash, liquid hand wash, alcohol-based sanitizers and mouthwashes) and proper communication of their virucidal benefits in engaging content to beat messaging sensitization, subject to evidence of proven efficacy in simplified manner staying true to information shared. This would allow consumers to be better informed and would also reinforce their overall compliance with public health recommendations. While in his original article Horton highlighted the need for broader understanding of managing COVID-19 outbreak in relation to non-communicable diseases, we conclude that a similar impact in the sphere of community infection control and prevention can be achieved through a coordinated and sustained effort between manufacturers of commercially available personal hygiene products, public health officials, and country regulatory authorities.

Conflicts of interest statement

All authors certify that they are paid employees of Unilever and its affiliates.

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