Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Hospital Infection 112 (2021) 121–123

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevier.com/locate/jhin

Letter to the Editor

SARS-CoV-2 mutational variants may represent a new challenge to society, but not to the virucidal armamentarium

Sir,

The inherent nature of RNA viruses, such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and other members of the *Coronaviridae*, favours the emergence of genomic mutations due to error-prone replication cycles [1]. It should not be surprising that we are now faced with newly emerging mutational variants of SARS-CoV-2. It has been reported [2] that SARS-CoV-2 acquires ~one new mutation in its genome every two weeks. Some of the recently emerging variants, including lineage B.1.1.7, have been found to be more transmissible at the population level [1]. The emergence of a more transmissible variant of a pandemic virus, such as SARS-CoV-2, naturally raises concern in the public-at-large. One concern is over the question of continued suitability of interventions used to mitigate viral dissemination. Fortunately, infection control and prevention (IPAC) interventions for limiting dissemination of original SARS-CoV-2 apply also to the newer variants. These include mask wearing, social distancing, and the monitoring of symptoms for those characteristic of the prodrome of COVID-19. It is expected that the vaccines designed for original SARS-CoV-2 will be effective also against the new variants, because these target the entire spike protein [1,3]. But what about targeted hygiene approaches for limiting indirect transmission of SARS-CoV-2 (i.e. transmission from contaminated fomites to susceptible oral, nasal, and ocular mucous membranes)? Will those targeted hygiene approaches that are effective for original SARS-CoV-2 [5] be effective for the new variants?

In order to answer this latter question, we need to consider: (1) the mechanism of action of microbicides commonly used against enveloped viruses; (2) empirical results comparing efficacy of microbicides for different coronaviruses; and (3) the heirarchy of susceptibility of pathogens to microbicides, which enables predictions to made regarding microbicidal efficacy.

Like all coronaviruses, SARS-CoV-2 and its variants are enveloped viruses. Viral envelopes are composed of phospholipids (fats) and proteins derived from the infected cell. The components of the viral envelope play multiple roles in initiating infection of a host cell [6]. These include, in chronological sequence, binding of virus to host-cell angiotensin-converting enzyme (ACE2) receptors, virus/cell membrane fusion, viral uncoating, viral genomic transcription and translation of new viral protein, maturation of progeny virions, and release of virus from the host cell. The latter occurs through the process of budding, in which new virions acquire virally modified host-cell membrane as part of the envelope. Disruption of the viral envelope by microbicides (Figure 1) impairs several steps in this sequence and, therefore, renders the virion incapable of initiating infection of a host cell. Any lipid-disrupting agent should, in theory, be effective against any enveloped virus [7]. Microbicides which cause protein denaturation (Figure 1) act by disrupting the interactions between virus spike proteins and the cellular ACE2 receptors. Additionally, protein-denaturing agents may act through impairment of the functions of the viral membrane, envelope, or nucleocapsid proteins. Certain microbicides act by causing genomic degradation (Figure 1). These mechanisms are equally applicable to a variety of enveloped viruses.

A wide range of formulated microbicidal actives incorporated into hygiene agents have been found to be effective against different members of the *Coronaviridae* [5]. In addition, efficacy of microbicides tested in hard surface inactivation studies and in suspension inactivation studies have demonstrated that there is little difference in efficacy for any given agent against different alpha- and beta-coronaviruses [5]. Taken together, these results provide a high degree of confidence that a hygiene agent effective for original SARS-CoV-2 will be equally effective against newly emerging mutational variants of the pandemic virus. As expected, these microbicidal actives also display virucidal efficacy against other enveloped viruses, including, but not limited to, influenza viruses (*Orthomyxoviridae*) and Ebola viruses (*Filoviridae*) [7]. Again, it is the mechanism of action of these agents that is crucial in conferring their efficacy for a broad range of enveloped viruses.

According to the hierarchy of susceptibility of pathogens to microbicides [7], all enveloped viruses, including SARS-CoV-2, other coronaviruses, newly emerging variants of SARS-CoV-2, as well as enveloped viruses from other virus families, should be equally susceptible to these microbicidal actives. In fact, this concept led the US Environmental Protection Agency to activate an Emerging Viral Pathogen Guidance for SARS-CoV-2 on 29th January 2020 [8], stating "This type of human coronavirus is an enveloped virus, meaning it is one of the easiest types of viruses to kill". This Emerging Viral Pathogen Guidance has been invoked on a number of occasions in the recent past

https://doi.org/10.1016/j.jhin.2021.03.013

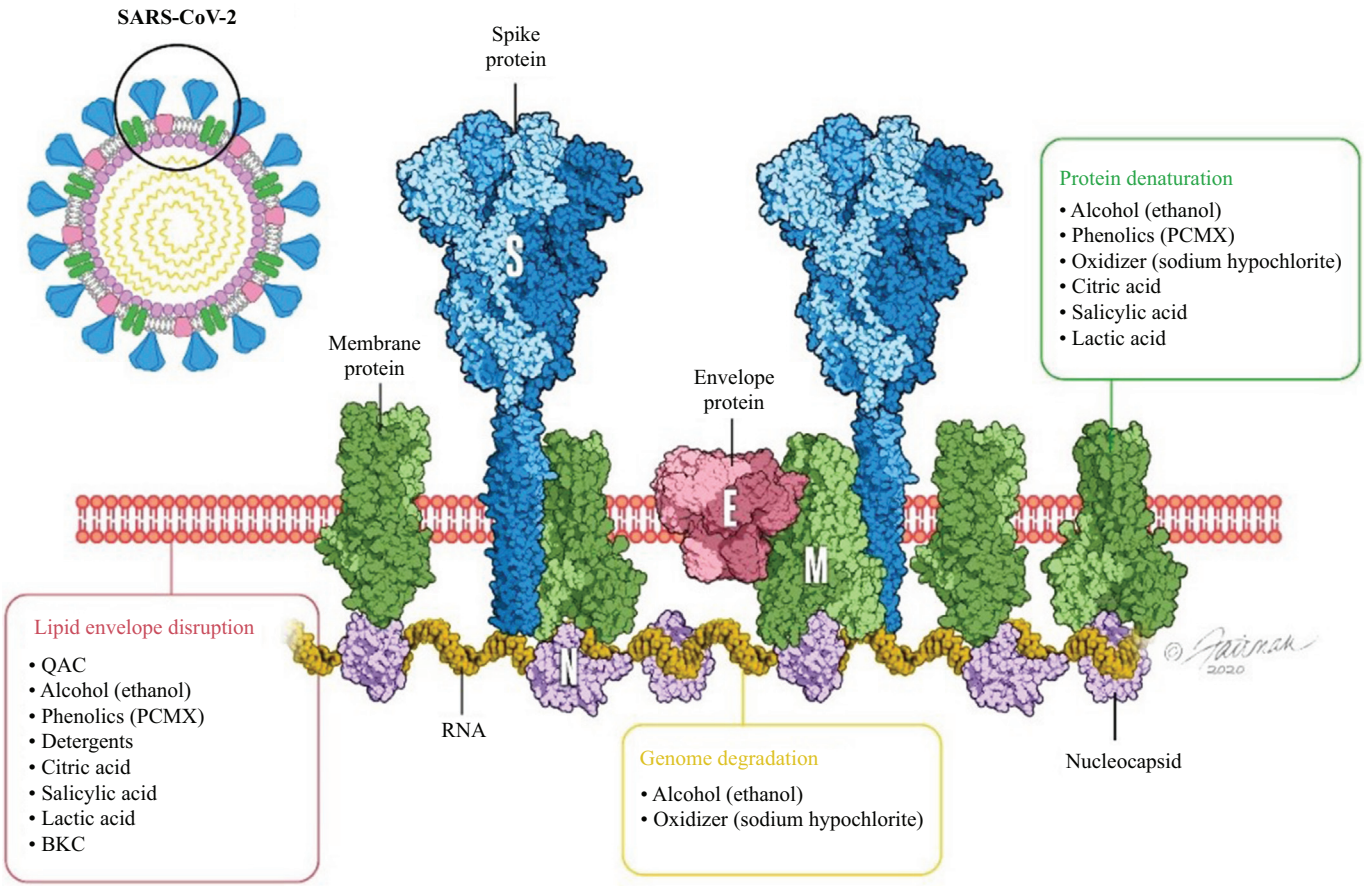

Figure 1. Schematic representation of SARS-CoV-2 showing ultrastructure and site of action of different classes of microbicides. BKC, benzalkonium chloride; PCMX, para-chloro-meta-xylenol; QAC, quaternary ammonium compound.

and is intended to facilitate IPAC in cases where empirical efficacy information for an emerging virus is not yet available.

It is hoped that the arguments presented in this commentary will provide assurance of the utility of targeted hygiene agents empirically demonstrated to possess virucidal efficacy against the original SARS-CoV-2 for IPAC of any newly emerging SARS-CoV-2 variants.

Author contributions

M.K.I.: conceptualization of the topic for the letter; research into topic; editing and approval. J.M.: conceptualization of the topic for the letter; editing and approval. R.W.N.: Authoring of first draft; editing and approval.

Conflict of interest statement

R.W.N. received a fee from Reckitt Benckiser, LLC for editorial assistance. M.K.I. and J.M. are employed by Reckitt Benckiser, LLC, which funded the writing of this letter.

Funding sources

Reckitt Benckiser, LLC provided funding for the research and writing of this letter.

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Available online 22 March 2021