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The Challenges and Opportunities for Innovative, Cheaper and Sustainable Public Health Compliant Disinfectant Technology - Trials and Tribulations of a Textile Industry in South of India and Its Initiatives to Locally Combat Contagions Including COVID-19 Management

Juluri R Rao*

Division of Applied Plant Science, Agri-Food and Biosciences Institute (AFBI), UK

Opinion and Commentary

The outbreak and the onset of the COVID-19 pandemics since December 2019 ushered in a new way of life to one and all world over. Face masked, hands washed frequently or gloved, socially distanced and face-off cyclic lockdowns. Working from home, living-in with your loved ones is a plus, yet begrudgingly acting up as teachers and being parents (home schooling) was a bitter sweet. With travel and hospitality frozen too, we were very near in civilization yet far from it! So, how do we reboot ourselves back to the future civilization from the pandemics?

Medical and scientific fraternity alike set about evolving diagnostic testing for the COVID-19, its emerging variants, "omics" data overdrives and production of COVID-19 vaccines. Pundits in science and public punters are conscious that conventional approaches to producing vaccine(s) could take years. Thus some of the pioneering virology labs in UK, USA, Europe and elsewhere were racing with time to produce a viable yet fast-track vaccine to counter COVID-19. Of course there were others amongst scientific and non-scientific community themselves who were contemplating bringing about novel means of preventative measures. It's a no brainer that necessity is mother of invention-as some of us became instant home inventors in improvised versions of masks, Personal Protection Equipment (PPEs). Then there were the re-inventors of a third kind who would want to "repurpose" antimicrobial formulations to also combat viral contagions on environmental surfaces. Such attempts were prompted in part by the historical data on virus models. COVID-19 is no exception, and could persist on a wide range of hard and soft surfaces for extended periods. All of these possibilities could impose new challenges to the containment of this vexatious community driven viral infection.

There still is an exponential demand for dealing with COVID-19 containment, prevention of dissemination, its treatment of those who contracted, since the outbreak of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). COVID-19 viral contagion causes severe pneumonia-like symptoms and its pandemic status was confirmed by the World Health Organization (WHO). To date roughly, COVID-19 has caused over 100 million confirmed infections and more than 2.5 million reported deaths in 223 different countries.

To contend with this global health crisis situation, development of several effective anti-SARS-CoV-2 vaccines will no doubt contribute to the control of the pandemic. To this end, the mRNA vaccines (Pfizer, AstraZeneca, Moderna, Johnson and Johnson among others), are after all a re-invented wheel! However emergence of SARS-CoV-2 strains (global origin variants: e.g. alpha, beta, gamma, delta etc.) with escape mutations that render some of the vaccines less effective and overall limited global supply of COVID-19 vaccines make a case for continued effort to identify therapeutic interventions. The mRNA vaccines have been there for a while, but found a re-purpose to deal with the COVID-19 control. Akin to new vaccines, discovering new drugs for treating infected COVID-19 patients is also laborious and time consuming. To counter punch this set-back, on-going researches have suggested that the "drug re-purposing" could be cheaper, and a fast-tracked effective means in treating COVID-19. For instance, one of the early studies [1] published in Nature, found that hydroxychloroquine and a drug called Remdesivir were effective in stopping COVID-19

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Correspondence:
Juluri R Rao, Division of Applied Plant Science, Agri-Food and Biosciences Institute (AFBI), Newforge Lane, Belfast, Northern Ireland, BT9 5PX, UK, E-mail: jr.rao@afbini.gov.uk

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spread *in vitro*. Of course, the oral use of hydroxychloroquine and azithromycin for COVID-19 treatment was deemed contentious, and falls out of scope for this commentary's focus. A more recent study published also in Nature [2] alludes on the urgent need for drug repurposing screens. This study identified chemical entities hidden amongst a plethora of approved for other diseases by the FDA (U.S. Food and Drug Administration) for the development of COVID-19 oral interventions. "The Repurposing, Focused Rescue, and Accelerated Medchem" (ReFRAME) containing nearly 12,000 small-molecule drugs have been shown to be appropriate for direct oral use in humans. They provide a rich resource to discover treatments that may be used as monotherapies or in combination with Remdesivir to further enhance treatment efficacy and tolerability towards COVID-19.

The above forensic style high throughput investigations for discovering re-purposed drugs is critical for "oral administrations and treatment regime" for COVID-19 patients. The flipside of drug discovery (or shortfall of it) is the "external application of viral disinfection agent" strategies in healthcare and common public environments. The latter particularly is highly relevant in developing and poorer countries where the general hygiene and infection prevention in their daily life is a formidable challenge and often is sadly inadequate. Any given viral aerosol dispersion in ambient air will be in very limited load i.e. low titers. However, due to high population density, the dynamics shifts towards total frequency of occurrence of the low-titer loads. Such viral particulate droplets are mainly known to arise via nasal and mouth (breathe, sneeze, cough and sputum-bodily discharges). The potential dissemination prevention of contagions have been problematic in the developing nations as their lockdowns, and social distancing, face mask and hand washing protocols often tend to cripple people's livelihoods.

It is common knowledge that hard surfaces in public high footfall areas (transport, shops, restaurants, and clubs etc.) would continue to harbor bacteria fungal or viral pathogens. In addition, the contagions' persistence both in hard and soft surfaces is not only longer but also burdensome for public health containment in developing and economically challenged countries. Most frequently encountered situations include soft surfaces such as people's attires; fabrics at home (possibly due to their less frequent automated washing and repeated re-use habits). Last but not the least, the pathogen load levels are substantive to severe in their healthcare setting (e.g. healthcare worker attire, wound dressings, apparels, bed linens, bed-bed privacy curtains, and semi-hard surfaces (e.g. upholstered furniture). Often they have higher in-patient and visitor footfall in their healthcare hospitals than in the developed world.

In the light of the above and the emerging COVID-19 crisis and its dissemination prevention management nuances on large populations as it were, a first lockdown in India (March 2020) in as much as it were global trend, prompted a Small to Medium sized Textile Entrepreneur (SME) www.lokkavachok.com set out a mini-scale pilot exploratory study to formulate a disinfectant that can be safely used on fabrics. The SME's early objective was to test the feasibility of a simple, health and safety compliant innovative formulation comprising basically repurposed chemical architecture that would act as potent antimicrobial coating to eliminate environmental pathogens and viral contagions persisting in soft surfaces (e.g. textiles, fabrics). The SME were inspired by the local governmental support for a good societal cause towards public health mitigation, and sought my scientific comments to contribute to the project inputs.

In this proof of concept model study, it was obvious that it is tedious and costly exercise to potentially test 1000's of drug candidates just for external use disinfectant purposes. A structure-function purpose was brain stormed. From the structural biology viewpoint, a number of FDA approved drugs whose chemical structures were linked to generic antimicrobial activity (e.g. disruption of cell membrane, life cycle process, protein-synthesis in bacteria, fungi, and DNA, RNA inhibition in viruses) were shortlisted, reviewed for dosage use concentration. The oral dosage administration of FDA approved drugs is normally set @ milligram/kilogram body weight basis. From viewpoint of SME's objective of sourcing FDA approved, health safety compliant chemical entities for external disinfectant use purposes, a minimum inhibitory concentration quantifiable expression will suffice for their qualitative antimicrobial activity. Thus commonly used FDA approved drugs at sub-lethal and nanomolar (nM) doses (10 nM to 4 nM) were trialed. The ensuing "commercial and confidential" unpublished results revealed that a number of FDA drugs had a remarkable antimicrobial potential at their nM use concentrations.

Using this trade secret data cue, initially the SME initiated an industrial process of coating the chosen chemical entities on fabric masks and tested them at various fabric testing organizations (see supplementary information). By this stage, SME met with set-backs as the local Indian market for antiviral coated mask was dominated by expensive (e.g. nano-silver) coated high-end masks. Despite the SME's Cheaper Antiviral Coated (AVC), media launch and other promos, it hit a road block. Due to the overcrowded antimicrobial mask market, and after wider consultations with local government and market analysts, the SME's choice was to re-formulate their product as multi-purpose antimicrobial fabric conditioners/ disinfectant market route for general public and the healthcare fabrics sector uptake. Interestingly, the above early trials and tribulations, led to formulation itself being 'repurposed'! The new formulation YUDEF (under non-disclosure, trade secret and patent pending agreements) contains QACs (Quaternary Ammonium Compounds) fortified with organic compounds referred to as AVC™ (structurally similar to approved FDA drugs - natural products derived from plants or microbes, negligible environmental burden of unwarranted antimicrobial resistances etc.). It thus has excellent chemical architecture: does not decompose during storage or use; no added heavy metals; but has molecular ion anchoring towards QUATS, innate cations of fabric/hard surface matrices.

YUDEF formulation is thus a specially designed liquid engineering composite to provide superior antimicrobial performance (>99%) for all types of textile and hard surfaces. It is readily water soluble and thus offers a value-added component for utility in emerging antimicrobial fabric conditioners and floor disinfectants range wherein the entrepreneurs identified a gap in the niche market for combating the environmental contagions. In the light of the urgency of the pandemics and contingency plans by local governments, the SME encouraged by their testing outcome (see supplementary data), have voluntarily donated 1000's of liters of their product for use in many consenting local exclusively built 1000-bed facility COVID-19 isolation hospitals and the users to date have deduced that YUDEF product is robust up to 50 washes of hospital linen laundering (private correspondence). Further in sit trials are in progress to extend the use for surface hygiene purposes in mass public transport systems etc.

Overview of the Commentary

Together with a Quaternary Ammonium (QUATS) based formulation referred to under a trade name YUDEF incorporating AVC™ elixir YUDEF - Anti Viral Coating (lokkavach.com) comprises nanomolar (i.e. sub-lethal levels than that of an oral dosage) FDA approved repurposed drugs. The structurally similar analogous natural products can be regarded as non-toxic, compliant to health and safety of the user, and were tested as antimicrobial coating on fabrics. The antimicrobial tests compliant to Indian and European standards (e.g. EN 14683) were done by independent testing laboratories (see Supplementary data PDF) on a 100% cotton fabric (144 gm^{-2}) supplied by www.lokkavach.com. The YUDEF formulation offered general environmental bacterial contagions as well as achieving 99.99% viral suppression. It acts as a multi-purpose antimicrobial agent either as a fabric conditioner or as surface disinfectant. This QUATS based formulation offers a simple means of managing the on-going waves of COVID-19 pandemics in many countries (e.g. India, Sri Lanka, Bangladesh, and other South East Asian countries) and help these economically challenged nations to comply with some reasonable hygienic forms of home management and to concomitantly maintain personal and community hygiene practices in terms soft and hard surfaces including healthcare scenarios. Such innovative trials and tribulations of industry (www.lokkavach.com) led science and technology, their challenges and opportunities should be commendably viewed as 'thinking globally (public health) and acting locally' (to combat pandemic contagions). A follow-on research will help the industry to underpin the science behind their practical working solution.

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