Coronaviruses and tea consumption: a potential strategy to help boost the immune system

The health-promoting benefits of tea consumption have been catalogued for centuries and are supported by modern intervention and epidemiological studies. Tea is produced from the tender leaves of the plant *Camellia sinensis*, which are harvested and processed into green, black or oolong tea leaves. Epidemiological studies suggest that the emergence of several diseases, especially cancer, cardiovascular diseases, diabetes, rheumatoid arthritis, etc. is significantly lower in the countries where 'tea culture' is more prominent than 'coffee culture'. Moreover, tea offers a positive effect on weight management, ageing, metabolic health, muscle endurance, bone strength and oxidative stress-mediated neurodegeneration such as Parkinson's disease. The health benefits of tea are linked to the presence of polyphenols and other phytochemicals. Notably, the flavonoid content in green and black tea can vary widely depending on the manner in which the leaves are processed.

For instance, the green tea catechins (GTCs) have been reported to prevent respiratory viral infections like Influenza, etc. In a clinical trial, the effects of catechins were tested for combating acute upper respiratory tract infections (URTIs) involving 270 health-care workers. Results showed that people who consumed the beverage for 12 weeks displayed a URTI rate of 26.7% in the placebo-controlled group (0 mg catechins and 100 mg xanthan gum), whereas 13.1% in the test group with high catechins (three daily doses of 57 mg catechins and 100 mg xanthan gum). The addition of polysaccharides (i.e. xanthan gum) prolonged the retention time of catechins by increasing the viscosity and hence promoting antimicrobial action. In this work we have documented the efficacy of catechins in the prevention of URTIs. Such a study also highlights the need for further research to validate the therapeutic potential of tea in controlling URTIs using large-scale clinical trials. GTCs, particularly epigallocatechin-3-gallate (EGCG), have been shown to help prevent viral infections from DNA and RNA viruses such as hepatitis B virus, herpes simplex virus, adenovirus, HIV, hepatitis C virus (HCV), rotavirus, enterovirus, ebolavirus, chikungunya virus, Zika virus, etc. Molecular docking studies further revealed that bioactive compounds like rutin or epicatechin-3-*O*-gallate (ECG) present in Green tea can potentially inhibit infections from dengue virus (DENV). Future studies on the anti-viral effects of GTCs will need to be carried out to validate their consumption as a viable therapeutic strategy and could reveal novel targets. At present, due to poor pharmacokinetic/pharmacodynamic characteristics, GTCs do not make good drugs. Hence, structure alterations, and synthesis of analogues are relevant targets of future GTCs research. The antiviral property of theaflavin, another flavanol found in black tea was also tested against HCV. Three of the main theaflavins found in black tea, namely TF1 (theaflavin), TF2 (theaflavin-3′-gallate), and TF3 (theaflavin-3,3′-digallate) were screened against HCV using human hepatoma Huh7 cell lines. The results showed that all three theaflavins were effective in inhibiting the early stage of HCV infection by acting directly on virus particles and preventing cell-to-cell transmission. Interestingly, combinatorial therapy of theaflavins with sofosbuvir and daclatasvir (FDA-approved drugs for HCV) showed a synergistic effect in preventing HCV infection, thus highlighting the therapeutic potential of theaflavins in the near future.

Certain nations have embraced the potential anti-viral properties of tea. For example, Sri Lanka started a 'Ceylon black tea' consumption campaign to help boost the immunity of its population against COVID-19. The Indian Tea Association (ITA) also encouraged consumption of black tea as an immunity booster due to its high theaflavin content. Tea is a rich source of polyphenols, particularly catechins, and the immunomodulatory effect of polyphenols is well-documented. The mechanism of immunomodulation is complex, where different polyphenols target and bind to one or more receptors on the immune cells. This triggers intracellular signalling pathways that ultimately modulate the host immune response. Dietary interventions have been proposed to affect epigenetic factors, such as the regulation of DNA methylation, histone modification and microRNA-mediated post-transcriptional repression. All of these can alter the expression of genes encoding key immune factors. Green tea extract especially was reported to amplify humoral immune response. Furthermore, an earlier study confirmed that tannic acid (with an IC_{50} value 3 μM) along with 3-isotheaflavin-3-gallate (TF2B; with an IC_{50} value 7 μM) effectively inhibited SARS-CoV $3CL^{Pro}$ activity. Puer tea or black tea showed greater inhibitory effect against $3CL^{Pro}$ than green or oolong tea extracts. In a separate study, it was noted that the ingredients found in 'Gene-Eden-VIR/Novirin' (a herbal antiviral patent) which include green tea extract as one of the components, can efficiently inhibit SARS-CoV $3CL^{Pro}$ action. A molecular docking experiment exhibited that theasinensin-D, theaflavin-3-*O*-gallate and oolonghomobisflavan-A were better inhibitors against SARS-CoV-2 $3CL^{Pro}$ than most repurposed anti-HIV drugs approved for COVID-19. Moreover, theaflavin might be an excellent SARS-CoV-2 RdRp inhibitor. The computational study along with docking using the catalytic site of the three-dimensional structure of RdRp protein, clearly revealed theaflavin as the pre-eminent compound among the other 83 compounds selected during that study, thereby subjecting it to further *in vitro* and *in vivo* confirmation.

In summary, previous experimental studies on DNA and RNA viruses, specifically beta-coronaviruses (i.e. SARS-CoV which shows a high sequence and functional similarity to SARS-CoV-2) and recent computational studies point towards the positive effect of tea against SARS-CoV-2 infection. However, extensive clinical trials must be conducted to prove this. Additionally, long-term consumption of green and black tea as a food supplement or wellness drink might be beneficial against other common viral infections. To provide definitive evidence on the beneficial effects of tea consumption on COVID-19, potential studies with biomarkers of exposure along with clinical trials are essential. Uncertainty surrounding the actual production of an effective anti-COVID-19 vaccine coupled with the uncertainty of a

nation's ability to provide enough vaccine to its population, make the concept of boosting immunity attractive. Not a sudden magic potion against SARS-CoV-2, tea could be an essential add-on to immunity-boosting strategies during this pandemic, which should be adequately studied.

Conflict of interest. The authors declare no conflicts of interest.

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MEETING REPORT

Science Academies' science leadership workshop

A week-long science leadership workshop supported by all three science academies in the country (Indian Academy of Sciences, Bengaluru, Indian National Science Academy, New Delhi, and The National Academy of Sciences, India, Prayagraj) was conducted through the virtual mode from 22 June to 28 June 2020. Touted as India's first science leadership programme, the workshop had arguably been one of the largest science events in the world in recent times in terms of participants, with 20,205 registered delegates alone that included both national and international participants.

The seven-day workshop featured fifteen inspiring talks by several well-known science leaders in the country and abroad. Besides, the workshop also included immersive sessions of eleven Young Science Leaders.

The workshop covered many important topics of science leadership that are often missed in traditional curricula, including critical thinking, group communication, problem solving, creativity and innovation, time management, risk-taking, mentoring, team work, coping up with mental stress as a scientist, flexibility, helping PhD students for emotional well-being, decision making, active listening and empathy, women in science, cross-cultural communication, lab culture, etc. All talks had the same title, 'on becoming a science leader', and the speakers shared their life journey, childhood inspirations, role models, and so on in a non-technical fashion, intending to inspire better leaders of tomorrow.

The workshop was unique in many dimensions. Out of 26 speakers, 15 were female, to ensure gender equality and uphold the spirit of 'women in science' – the theme of this year's science day by the union government. Gender ratio among speakers relayed a subtle yet profound message that women can be as good science leaders as men. Organizers also ensured that each session had one male and one female moderator. As the workshop was held through the online mode and live-streamed through YouTube, tens of thousands of people worldwide participated in the sessions. All sessions were two-way, with the audience having the option to pose their questions and get it answered by the speakers. All talks of this workshop were archived and curated at YouTube for the benefit of posterity and the people with internet connectivity issues (https://bit.ly/Science-Leadership). The organizers also released an Android app to facilitate offline access to the generated content. Several sessions of the workshop highlighted the importance of ethics in science, and a final exam was conducted in such a manner to underline this vital topic. The so-called 'exit exam' was based on academic honour code, and the certificates required self-declaration that the candidates passed the workshop – first of its kind in the country. The organizers also ensured that certificates were fool-proof with digital validation feature.

Despite massive outreach, the organizing team consisted of just two persons and nine student volunteers, indicating how we could leverage the power of information technology. In terms of finances, the workshop had been a zero-budget programme with no grants sought from the academies or elsewhere, including honorariums (for both speakers and coordinators). Also, as there were no travels – especially air travels – associated with this workshop (the workshop had four international speakers and thousands of international participants), the overall carbon footprint remained almost zero. COVID-19 lockdown period has forced us to move the workshop to a virtual mode, which unexpectedly came with many additional advantages, especially environmental consciousness and transition towards carbon neutrality. We believe workshops like this might become the 'new normal' in the post-COVID-19 era, to continue the momentum of environmental sustainability that we learned during the lockdown period, way forward in years to come.

The workshop also paved the way for two important extension programmes. The first is a country-wide 'Virtual Internship with Science Leaders' (VISL) programme wherein students from school grade seven to PhD can find their mentors among established Young Science