Letter to the Editor

Pharmacopoeia roles and responses: A systemic resilience approach to COVID-19 pandemic

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A B S T R A C T

The Coronavirus Disease (COVID-19) is sweeping around the world at a rapid pace resulting in severe health crises across the globe. The pandemic condition has forced the government, regulatory authorities, bio/pharmaceutical industry, and healthcare system to take novel measures to address the crisis. The race for development of medicines and vaccines for treatment of COVID-19 is well under way and regulatory authorities are making efforts to safely deliver it into hands of public. As ever, pharmacopoeias played an active role in providing a framework of standards for the development, manufacturing, and quality of life-saving COVID-19 related medicines. The COVID-19 crisis has compelled the pharmacopoeias to redefine their role and show unprecedented levels of flexibility in extending their services to the stakeholders, developing new drug standards, and simultaneously ensuring the safety of their staff. During this pandemic, pharmacopoeias operated in a triangular chain system with regulators and pharmaceutical manufacturers to evaluate potential products for treatment of COVID-19. The present article provides an insight on the roles, challenges, and responses of the pharmacopoeias to deal with the current situation due to COVID-19 and emphasizes on new opportunities for collaborations to set standards for COVID-19 related drugs.

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1. Introduction

In January 2020, World Health Organization (WHO) has declared novel coronavirus (COVID-19) as a world health emergency and in March 2020 the same was declared as a pandemic, the highest level of world emergency. As of December 2021, most of the cases of COVID-19 were reported from the USA, India, Brazil, and Russia (WHO, 2020). During the initial phase of pandemic, various repurposing drugs have been attempted for treatment and management of COVID-19 cases; however, owing to limited clinical evidence their use was restricted (Jean et al, 2020). The pandemic condition has forced the governments, regulatory authorities, pharmaceutical industry, and healthcare system to take novel measures to address the crisis. The ongoing COVID-19 disaster has led to a dramatic global impact on the pharmaceutical industry operations and pharmaceutical sectors are struggling hard to maintain productivity, workforce, securing operations, and mobility thereby limiting access to essential medicines for end users (Ayati et al, 2020). Aside from responding to the immediate threat, the organizations have to adapt quickly to ensure that they can be pliant to disruption and can work in a more agile way in the post-covid environment (Hiscott et al, 2020).

Responding to the COVID-19 pandemic, the health authorities are also compelled to work in a way that is normally reserved for natural disasters. Several national and international organizations are working in collaborations to develop new policies, procedures, and therapeutic interventions (Hiscott et al, 2020). Their working is now based on fast-track approval of essential drugs, emergency regulations, and mutual agreement to deliver the drugs safely into hands of patients (Harrison, 2020). In the sphere of public health, pharmacopoeias have the responsibility to ensure quality of the marketed medicinal products to help protect the patients from adulterated and counterfeited medicines. Pharmacopoeias discharge this responsibility by defining the quality standards of the active pharmaceutical ingredients (API) and finished pharmaceutical preparations (FPFs). In addition, pharmacopoeia bodies establish and distribute reference standards for assessment of the quality of medicines following monograph specifications. For the process of standards’ setting, pharmacopoeia bodies consult and collaborate with regulatory authorities, health authorities, pharmaceutical industry, and other stakeholders. Compliance with the pharmacopoeia standards is legal regulatory requirement in countries and regions where pharmacopoeia is applicable (Wiggins and Albanese, 2020a; 2020b).

Current COVID-19 pandemic has posed a serious challenge to the working of pharmacopoeia bodies globally and pharmacopoeias have prioritized their activities and functions to support the healthcare system by assuring availability and access to the...
drug standards for the stakeholders. Present article covers the perspective in redefining the roles of pharmacopoeias during COVID-19 realities with respect to their challenges, responses, and opportunities to strengthen the drug standards to deal with the pandemic.

2. Pharmacopoeias: Global perspective

WHO has compiled an index of the pharmacopoeias published across the globe. As per the latest index compiled, there are as many as 60 pharmacopoeias published around the world (WHO, 2021b). These pharmacopoeias are embedded in their own national or regional regulatory legislation and thereby making them legally binding to comply with (Wiggins and Albanese, 2020a). For example, the European Pharmacopoeia (Ph. Eur.) is mandatory when requesting marketing authorization in the member states of European Pharmacopoeia Commission, as prescribed in the European Union Directives 2001/83/EC and 2001/82/EC (Stemplewski, 2018). Similarly, the Indian Pharmacopoeia (IP) is the official book of drug standards as per the second schedule of the Drugs and Cosmetics Act, 1940 and Rules 1945 there under for obtaining marketing authorization in India (Malik, 2014). The Japanese Pharmacopoeia (JP) is an official document that defines the specifications, criteria, and standard testing methods necessary to properly assure the quality of drugs in Japan, based on Paragraph 1, Article 41 of the Law on Securing Quality, Efficacy, and Safety of Products including Pharmaceuticals and Medical Devices (Kameyama et al, 2019). Also, the United States Pharmacopeia (USP) is used to control the quality of drugs distributed in the United States, as prescribed in Sections 201(g) and 501(b) of the Federal Food, Drug, and Cosmetic Act (USP, 2021b). Further information in this regard is published elsewhere and is beyond the scope of present article.

3. COVID-19 pandemic: roles and responses of pharmacopoeias

The resilience of pharmacopoeia organizations worldwide is being tested to combat the new challenges posed by COVID-19. Though the pharmacopoeia bodies constantly made efforts to remain operational and to support pharmaceutical industry, regulatory authorities, and health authorities to manage the pandemic situation, new challenges have emerged that need to be responded by each of the pharmacopoeias. These include, but not limited to, continuing their operations with respect to monograph development and modernization through public consultations, maintaining supply chain of reference standards, and above all ensuring the safety of their staff.

In response to the COVID-19 pandemic, WHO under umbrella of International Meeting of World Pharmacopoeias, initiated global pharmacopoeia alert meetings with participation of various pharmacopoeias like Brazilian, British, European, Indian, International, Japanese, Mexican, and United States. As per the information displayed on the WHO website, pharmacopoeial alerts are a mechanism that permits rapid discussions between pharmacopoeias to respond to pressing public health need (WHO, 2021a). The goal of this alert was knowledge sharing among the pharmacopoeias to figure support strategies for drug manufacturers, regulators, and other stakeholders in response to current pandemic along with providing support on medicines vital to the COVID-19 response. These discussions were immensely useful for individual pharmacopoeias to learn from the experiences of other pharmacopoeias to better plan innovative strategies to continue with their functions during the challenging time. Pharmacopoeia alerts also provided a scope to follow the harmonized approach for monograph development and revision in addition to the development of new drug standards particularly those used in treatment, management, and prophylaxis of COVID-19. Such interactions are expected to help ensure the availability of affordable quality medicines for COVID-19 in days to come.

Globally, the pharmacopoeias have discretionary actions and different working approaches in response to COVID-19 pandemic. Confronted with COVID-19 pandemic, British Pharmacopoeia (BP) worked closely with Medicines and Healthcare products Regulatory Agency (MHRA) to anticipate and meet health product needs. This involved maintaining access to drug standards and developing new standards (BP, 2021). Likewise, Ph. Eur. considered the fact that availability and access to quality medicines is more important and accordingly has taken several measures. Ph. Eur. collaborated with BP to make pharmacopoeia texts (monographs, general chapters, appendices, and supplementary chapters) available to users (BP, 2021). Similarly, IP was actively engaged in providing important healthcare-related services to its users. The supply of IP reference standards and impurity standards remained unimrupted to all the stakeholders including pharmaceutical manufacturers and drug testing laboratories so that there is no hurdle in the release of medicines into the market. IP also provided its support to health authorities by extending its analytical laboratory for testing of the drugs received from various government agencies including the National Health Programmes (NHPs) (IP, 2021). Technical queries related to IP monographs continued to be addressed after consultation with the Expert Working Groups through virtual meetings. In order to strengthen the quality standards of the COVID-19 related drugs, several monograph revisions were initiated. Considering the requests of the pharmaceutical manufacturers, publication of the IP Addendum was also extended by six months. This extension helped pharmaceutical industry to be better prepared for ensuring compliance with the new drug standards included therein (IP, 2020). International Pharmacopoeia (Int. Ph.) was engaged in speeding up the development, production and distribution of vaccines, diagnostics, and therapeutics for COVID-19. The JP restricted its work to 30% in accordance with Japan’s emergency statement; although, JP has adapted to support industry and other stakeholders as the need arises. The Pharmacopoeial Discussion Group remained functional to work on pharmacopoeial harmonization of general monographs and excipients. Specific measures were taken by the JP along with the Ministry of Health for enforcing the availability of disinfectants and priority review of COVID-19 related drugs and products (JP, 2021). The USP played a critical role in the public health response to COVID-19 by providing uninterrupted access to USP’s quality standards and support services to manufacturers, scientists, healthcare practitioners, and regulatory bodies (USP, 2021a). Various initiatives were taken by the USP to support industry e.g., shortening the development time of possible treatments, giving 6 months complimentary access to USP-NF online, extending implementation, and comment period for USP publications by 6 months, etc. The USP also offered technical assistance to industry on vaccine development, antibody therapies, and antiviral therapies and scaling up production of approved therapeutics such as secondary medications needed for patients on ventilators (USP, 2021a). USP has also published recommendations for compounding alcohol-based hand sanitizers for use during shortages associated with the COVID-19 pandemic.

4. COVID-19: challenges and opportunities for pharmacopoeias

COVID-19 has displayed the most severe impact on every sphere of the health sector, including hospitals, disease prevention, treatment, management, policy making, pharmaceutical industry, and drug regulation (Nicola et al, 2020). Pharmacopoeias worldwide have responded to the crisis using a range of regulatory instruments, including maintenance of supply chain of reference standards, interaction with the industry and regulators, develop-
ment of new standards, and taking appropriate measures for staff safety. The biggest challenge before the pharmacopoeias was that there was no approved therapy or vaccine available for diagnosis, treatment, and prevention of COVID-19, and therefore, the action points and work areas were not defined for the pharmacopoeias.

4.1. Comparative status of drug monographs in pharmacopoeias

In order to have concrete efforts to deal with the challenges posed by COVID-19 and to co-ordinate the activities of different pharmacopoeias, WHO has organized pharmacopoeia alert meetings on regular basis and these meetings have contributed to the compilation and publication of the monograph status of different pharmacopoeias for medicines critical to COVID-19 response. In this regard, a dashboard has been developed and displayed on the websites of the USP and WHO for public access (USP, 2021; WHO, 2021). It is observed from this dashboard that the USP (n=138) lists the maximum number of monographs, followed by BP (n=131) and IP (n=99) while Vietnamese Pharmacopoeia (n=27) has listed the minimum number of monographs. These differences in monograph numbers are to be attributed to variations in policies and related regulations across the pharmacopoeias (Kameyama et al, 2019). USP has a policy of including standards for all drugs, including drug formulations that are legally marketed in the USA whereas the JP focuses primarily on drugs that are essential for health care and medicinal treatment rather than all drugs marketed in Japan. Likewise, the Ph. Eur. has historically focused on the development of API and excipients monographs while IP gives priority to those drugs which are used in the NHPs and critical for treatment of diseases prevalent in India. This comparative information on status of drug monographs in different pharmacopoeias would be found useful by the pharmaceutical manufacturers, drug regulators, and health authorities to help in drug development and thereby responding to urgent public health needs during present global pandemic. Monograph deficiencies in the individual pharmacopoeias could be taken up by them as the starting point for setting drug standards based on the specific monograph inclusion criteria adopted by the individual pharmacopoeias.

4.2. Status of disinfectant monographs in pharmacopoeias

Sanitizers containing 70% alcohol have been recommended for sanitization of hands to avoid infection due to COVID-19 and two types of alcohols used in the manufacture of hand sanitizers are either ethyl alcohol or isopropyl alcohol. Similarly, a 1% solution of sodium hypochlorite has also been recommended in India for cleaning surfaces to prevent the spread of COVID-19 infection. USP played an integral role in issuance of guidance on the formulation of alcohol-based sanitizers to help authorities to contain

### Table 1

Comparative status of disinfectant monographs in IP, USP and BP.

| Category               | Molecule                        | Monographs                              | IP 2018 | USP 43 | BP 2021 |
|------------------------|---------------------------------|-----------------------------------------|---------|--------|---------|
| Skin Disinfectant      | Isopropyl Rubbing Alcohol       | Isopropyl Rubbing Alcohol               | ✓       | ✓      | X       |
| Surgical Spirit        | Surgical Spirit                 | ✓                                       | ✓       | ✓      | ✓       |
| Antiseptic             | Benzalkonium Chloride           | Benzalkonium Chloride                   | ✓       | ✓      | ✓       |
|                        | Benzalkonium Chloride Solution  | ✓                                       | ✓       | ✓      | ✓       |
| Bronopol               | Bronopol                        | ✓                                       | ✓       | ✓      | ✓       |
| Chlorhexidine          | Chlorhexidine Acetate           | ✓                                       | ✓       | ✓      | ✓       |
|                        | Chlorhexidine Acetate Topical Solution | X                                    | ✓       | ✓      | ✓       |
|                        | Chlorhexidine Irrigation solution | X                                    | ✓       | ✓      | ✓       |
|                        | Chlorhexidine Gluconate Solution | ✓                                       | ✓       | ✓      | ✓       |
|                        | Chlorhexidine Gluconate Topical Solution | X                                    | ✓       | ✓      | ✓       |
|                        | Chlorhexidine Hydrochloride     | ✓                                       | ✓       | ✓      | ✓       |
| Chlorocresol           | Chlorocresol                    | ✓                                       | ✓       | ✓      | ✓       |
| Chloroxylenol          | Chloroxylenol                   | ✓                                       | ✓       | ✓      | ✓       |
|                        | Chloroxylenol Solution          | ✓                                       | ✓       | ✓      | ✓       |
| Dequalinium            | Dequalinium Chloride            | ✓                                       | ✓       | ✓      | ✓       |
| Hydrogen Peroxide      | Hydrogen Peroxide Solution (22 vol) | X                                    | ✓       | ✓      | ✓       |
|                        | Hydrogen Peroxide Solution (100 vol) | X                                    | ✓       | ✓      | ✓       |
|                        | Hydrogen Peroxide Concentrate   | X                                       | ✓       | ✓      | ✓       |
|                        | Hydrogen Peroxide Topical Solution | X                                    | ✓       | ✓      | ✓       |
|                        | Hydrogen Peroxide Solution (6%) | X                                       | ✓       | ✓      | ✓       |
|                        | Hydrogen Peroxide Solution (30%) | X                                       | ✓       | ✓      | ✓       |
|                        | Hydrogen Peroxide Solution (3%) | X                                       | ✓       | ✓      | ✓       |
| Iodine                 | Iodine                          | ✓                                       | ✓       | ✓      | X       |
|                        | Alcoholic Iodine solution       | X                                       | ✓       | ✓      | ✓       |
| Phenol                 | Phenol                          | ✓                                       | ✓       | ✓      | ✓       |
| Phenylmercuric Nitrate | Phenylmercuric Nitrate          | ✓                                       | ✓       | ✓      | ✓       |
| Potassium Permanganate | Potassium Permanganate          | ✓                                       | ✓       | ✓      | ✓       |
| Povidone               | Povidone-Iodine                 | ✓                                       | ✓       | ✓      | ✓       |
|                        | Povidone-Iodine Solution        | ✓                                       | ✓       | ✓      | ✓       |
| Quiniodochlor           | Quiniodochlor                   | ✓                                       | ✓       | ✓      | ✓       |
| Thiomersal             | Thiomersal                      | ✓                                       | ✓       | ✓      | ✓       |
| Thymol                 | Thymol                          | ✓                                       | ✓       | ✓      | ✓       |
| Pharmaceutical Aid     | Chloroform                      | ✓                                       | ✓       | ✓      | ✓       |
|                        | Cresol                          | ✓                                       | ✓       | ✓      | ✓       |
|                        | Dehydroacetic Acid              | ✓                                       | ✓       | ✓      | ✓       |
|                        | Ethanol                         | ✓                                       | ✓       | ✓      | ✓       |
|                        | Ethanol (95 Per Cent)           | ✓                                       | ✓       | ✓      | ✓       |
| Isopropyl Alcohol      | Isopropyl Alcohol               | ✓                                       | ✓       | ✓      | ✓       |
| 1% Sodium hypochlorite solution | Dilute Sodium hypochlorite solution | X                                    | X       | ✓      | ✓       |
|                        | Strong Sodium hypochlorite solution | X                                    | X       | ✓      | ✓       |
|                        | Sodium hypochlorite solution    | X                                       | ✓       | ✓      | ✓       |
|                        | Sodium hypochlorite Topical solution | X                                    | X       | ✓      | ✓       |
| Category not mentioned | Glutaraldehyde                  | Glutaraldehyde Solution                 | ✓       | ✓      | ✓       |
|                        | Strong Glutaraldehyde Solution | ✓                                       | ✓       | ✓      | ✓       |
spread of COVID-19 which is essentially in line with the guidance available from the WHO (WHO, 2010). This guidance intended to address the shortages of alcohol-based hand sanitizers and was not official in nature.

In addition to the drug monographs, pharmacopoeias also prescribe standards for various disinfectants, and a comparison of such monographs in IP, USP, and BP is given in Table 1. This comparison shows that there are variations in the listing of disinfectant monographs among the pharmacopoeias. Based on this comparison, individual pharmacopoeia may also initiate the development of monographs for the key disinfectants that would help ensuring the quality of the marketed disinfectant products. Also, when we analyzed the requirements of disinfectant monographs like isopropyl alcohol and isopropyl rubbing alcohol among three pharmacopoeias, differences were observed in the test methods and the specifications (data not shown). In order to address these differences, IP initiated monograph revision and harmonization for isopropyl alcohol and isopropyl rubbing alcohol. Methods and specifications of UV test and benzene were included in isopropyl alcohol monograph. Similarly, a gas chromatography based test for related substances was included in isopropyl rubbing alcohol to detect possible impurities in the hand sanitizers. This becomes important as an alert for possible contamination of methanol in hand sanitizers has been issued by the USFDA (FDA, 2020) and gas chromatography would enable detecting such adulterations in marketed products.

4.3. Quality specifications of COVID-19 related drugs

Several drugs, including anti-malarial drugs (Hydroxychloroquine and Chloroquine), anti-parasitic drugs (Ivermectin), antibiotics (Azithromycin), etc. have been proposed as a potential treatment of the COVID-19 (Alsuliman et al, 2020) though limited clinical evidences are available to support these claims. Among the monographs available for these drugs in different pharmacopoeias, there are variations with respect to their test parameters, test methods, and acceptance criteria. Here we elaborate such variations by taking an example of Hydroxychloroquine, a drug suggested as possible treatment against the COVID-19 (Cortegiani et al, 2020). IP took an initiative to revise the standards for Hydroxychloroquine API in order to ensure the monograph standards are updated and harmonized. Table 2 summarizes a comparison of Hydroxychloroquine API specifications available in the IP, USP, and BP. It is evident from this comparative analysis that there are differences in these monographs among the three pharmacopoeias and therefore, IP made efforts in consultation with the industry to update and harmonize Hydroxychloroquine API monograph. This harmonization is primarily focused with respect to the test for related substances and assay. IP adopted stability indicating HPLC methods for these tests. Similar harmonization in the quality standards laid down by various pharmacopoeias may contribute to globalization of the drug market and decrease the burden on the manufacturers and testing laboratories to perform analytical procedures using different methods and acceptance criteria and thereby making them accessible to the end-user (Kameyama et al, 2019).

4.4. Development of pharmacopoeia monographs

In current scenario, various pharmaceuticals have been approved by the drug regulatory authorities and are available in market for emergency use by the patients to treat COVID-19. Pharmacopoeias started working on development of standards for such drugs with industry and stakeholder support. These include, but not limited to, Remdesivir and Favipiravir, for which monographs have been developed by the IP and the Int. Ph. In India, IP has taken up priority activity of monograph development for Remdesivir and Favipiravir with support of the pharmaceutical industry as several of the Indian manufacturers have been granted marketing authorization for these drugs. Due to pandemic situation, IPC organised virtual consultations with manufacturers, regulators, and other stakeholders beside inviting public comments by hosting draft specifications on IPC website. These consultations resulted in finalization of specifications for APIs and FPPs of both drugs with generic attributes that

| Parameter | IP 2018 | USP 43 | BP 2021 |
|-----------|---------|--------|---------|
| Assay Limit | 98.0 to 102.0% | 98.0 to 102.0% | 98.0 to 102.0% |
| Identification | IR, Sulphate Test | UV, IR, Sulphate Test | IR, Sulphate Test |
| Appearance of Solution | NA | NA | Solution is clear and not more intensely coloured than reference solution Y7 |
| Related Substances | By- HPLC | By- Visualization | By-HPLC |
| | desethyl Hydroxychloroquine- NA | | Impurity C* - NMT 0.4 % |
| | hydroxychloroquine- NMT 0.4% | | Impurity B* - NMT 0.15% |
| | O-sulphate- NMT 0.15% | | Total Impurity - NMT 0.6 % |
| | 4,7-dichloroquinoline- NMT 0.1% | | |
| | Single Impurity- NMT 0.1 % | | |
| | Total Impurity - NMT 0.6 % | | |
| Chlorides | 350 ppm | NA | NA |
| Heavy Metals | NMT 20 PPM | NA | NA |
| Sulphated Ash | NMT 0.1% | NMT 0.1% | NMT 0.1% |
| LOD | NMT 2.0% | NMT 2.0% | NMT 2.0% |
| Assay | By HPLC | By- UV | By HPLC |
| Storage | Store Protected from light | Well closed, light-resistant Containers | Detector- 254 nm |

IR, infrared spectroscopy; UV, Ultra-violet Visible spectroscopy; HPLC, High Performance Liquid Chromatography; PPM, Parts per Million; NMT, Not more than; NA, Not Available.

* 2-[[4RS]-4-[[7-chloroquinolin-4-yl]amino]pentyl]amino]ethanol.
† 2-[[4RS]-4-[[7-chloroquinolin-4-yl]amino]pentyl]ethylamine ethyl hydrogen sulphate.
can assess quality of all the marketed products in India. Monographs on Remdesivir and Favipiravir have been published and become official in IP Addendum 2021 and with this IP became the first pharmacopoeia having monographs of these drugs.

4.5. Establishment of reference standards

IPC also identified the need for establishment of new reference standards to support IP monographs of COVID-19 related drugs. Manufacturers were requested to donate physical materials to be considered for use as reference standard after their evaluation. Candidate materials were tested in multiple collaborative laboratories along with IPC lab following the predefined protocol based on the analytical procedures given in IP monographs along with other methods for rigorous characterization of the candidate materials. Based on the lab testing data the materials were assessed for their suitability as IP reference standard and released for use after approval. These reference standards include: Favipiravir, Hydroxychloroquine Sulphate, Azithromycin, Doxycycline Hydrochloride, Ivermectin, and Dexamethasone. Once adopted by the IP, official reference standards became available for distribution and use in pharmaceutical analysis according to the corresponding monograph of the IP (IP, 2021). These reference standards will support the monograph specifications in the IP and are intended to be used as primary standards for physical and chemical tests and assays described therein.

5. Conclusions

The development in pharmaceutical sector is traditionally slow and change is only possible when there is an external force. This situation exactly happened during COVID-19 pandemic when regulators encouraged pharmaceutical manufacturers for possible collaborations. Although, regulatory authorities adopted fast track approval pathways but careful post implementation review is important to ensure the safety and efficacy of the medicines. In order to supplement these developments, pharmacopoeias also adopted several novel processes to help regulatory and health authorities by setting new drug standards and initiating monograph revisions for ensuring availability of quality medicines for treatment and management of COVID-19 patients.

Quality specifications of pharmacopoeias comprise of a set of appropriate tests and specifications that confirm the identity, purity, safety, and strength of the medicinal products to enable assessment of the quality of marketed products. The WHO document on ‘Good Pharmacopoeial Practices’ defines a pharmacopoeia’s core mission as protecting public health by creating and making available public standards to help ensure the quality of drugs (WHO, 2016). The existence of such pharmacopoeial specifications and requirements is of utmost importance for the proper functioning of regulatory control of drugs in a given setting. Pharmacopoeia functions are driven by collaborations with the pharmaceutical manufacturers, drug testing laboratories, drug regulatory authorities, research institutions, academia, and the public.

Pharmacopoeial specifications and requirements represent the basis of the technical norms for regulatory drug control in a given country or region. There are obvious differences among the pharmacopoeias with respect to the listing of the drug monographs as well as the specifications prescribed in the individual monographs. As pharmacopoeias continue to grapple with the unprecedented challenges thrown up by the COVID-19, a specific area of concern has been the uncertainty surrounding the impact of the COVID-19 pandemic on pharmacopoeia functions and operations that needs to be redefined. During the COVID-19 pandemic when there was a worldwide lockdown to contain the spread of infection, functions of pharmacopoeia bodies were also severely hit. Pharmacopoeias were compelled to adopt innovative approaches to remain operational and to meet the challenges imposed by the COVID-19. Despite all the hardship faced by the pharmacopoeias, commitment has been shown to extend support to the users for different pharmacopoeia services particularly for continuous supply of reference standards, development and modernization of monographs, and resolution of the technical queries on the pharmacopoeia texts. Though COVID-19 had forced the staff to work remotely, new solutions were quickly adopted to continue with pharmacopoeia operations and to extend services to the users.

During the COVID-19 crisis, we have witnessed a worldwide upsurge in the pharmaceutical and clinical research to develop new therapeutics and prophylactic candidates for the COVID-19 which have been shown to produce beneficial effects in different settings; however, little scientific and clinical evidence are available to support these claims. Efforts to develop vaccine candidates are also well underway yet projected to take considerable time (Alsuliman et al, 2020). This has resulted in the search for repurposed drugs to treat and reduce deaths from COVID-19. In such a scenario, the role of pharmacopoeia becomes important to help its stakeholders in providing solutions through the development of new monographs, revision of existing specifications and requirements, monograph modernization, harmonization, and establishment of new reference standards to support the pharmacopoeia specifications. This demands industry for the development of monograph specifications for new drugs and their physical reference standards. The pharmacopoeias under the current pandemic circumstances have wider functions and greater responsibilities than ever before. In order to meet the challenges of the current COVID-19 pandemic, there is need to establish harmonized monographs of the drugs being used in its treatment or management. The availability of harmonized monographs would be a big step forward to make available the affordable generic versions of such drugs because differences in the pharmacopoeia and regulatory requirements in different countries and regions are the well-known facts for cost increases and delayed access to drugs (Harrison, 2020). Harmonization of pharmacopoeia standards would reduce the burden associated with redundancy in regulatory drug testing and is the need of the hour to better combat the threat posed by the COVID-19. The development of harmonized monographs essentially requires understanding the differences across individual pharmacopoeias and to identify preferred areas for collaboration among the pharmacopoeias. For efficient collaboration among the pharmacopoeias, it is essential to prioritize the areas of collaboration and make the best use of the limited resources available with each pharmacopoeia.

This article also made an attempt to summarize the availability of selected pharmacopoeial monographs and their specifications among major pharmacopoeias for the drugs being used for COVID-19 treatment across the globe. The differences in the listing of drug monographs are evident from the WHO dashboard. Although, deciphering the detailed differences in monograph specifications among the pharmacopoeias was beyond the scope of this article, we have summarized the differences among the IP, BP, and USP with the example of Hydroxychloroquine in Table 2. It is evident that assay limit and related substances test limits have been harmonized, however testing methods still differ among the three pharmacopoeias. This comparison highlights the importance of analyzing the specifications of monographs listed among the pharmacopoeias and understanding the source of the differences in specifications before harmonization of pharmacopoeia text is initiated. Such an analysis would be of utmost importance for providing the technical inputs required as a step toward further convergence of pharmacopoeia standards for COVID-19 related drugs. Further, a closer co-operation with the health officials, drug...
regulatory authorities, and pharmaceutical industry experts must be considered to improve the specifications and to speed-up the revision of monographs.

We would like to emphasize here that there are currently no authorized medicines to prevent or treat COVID-19 and therefore, the drug monographs discussed in the present article shall not be inferred as recommendations for the treatment of COVID-19. However, the strategies discussed in the present article would be a good starting point to frame pharmacopoeia policies and procedures towards better addressing the challenges posed by COVID-19 global pandemic.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Disclaimer

The views expressed in this article are the personal views of the authors and shall not be understood or quoted as being made on behalf of or reflecting the position of the Indian Pharmacopoeia.

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