

Review Article

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COVID-19: unprecedented challenges for Indian pharmaceutical industry and pharma emerging markets

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ABSTRACT

WHO has declared the present outbreak of a new corona virus disease (COVID-19) as a global pandemic. The impact of novel COVID-19 epidemic is uncertain and unpredictable, which is also a challenging phase for the pharmaceutical industry across the globe. The rationale of this article is to compile existing research and published data and identify the various challenges among the pharmaceutical sector in India and other developing countries. To overcome from present epidemic effects such as increase in medicine price, disruption in the pharmaceutical supply chain, balancing between IPR and access to innovation and regulation on counterfeit medicine in developing countries, the certain possible strategies and solutions are discussed. The present article also emphasized the solidarity and global cooperation among developing countries to strengthen the pharmaceutical operations across India and other developing countries to meet the current demand during COVID-19 pandemic.

Keywords: COVID-19, Pandemic, Pharmaceutical supply chain, Current pharmaceutical research trend, Access to medicine, Intellectual property right

INTRODUCTION

During these unprecedented times of corona virus (COVID-19) pandemic, the pharmaceutical industry is also continuously grappling with new challenges at global level. Indian pharmaceutical sector stands world third-largest drug producer in terms of volume and positioned fourteenth rank in terms of value.¹ Indian pharmaceuticals manufacture more than 60% of global vaccine requirement. India supplies affordable and low-cost generic drugs to millions of people throughout the globe with more than 319 USFDA, and MHRA approved plants. Indian generic manufacturer produces the 33% of the total pills consumed in the US and similarly Indian pharma companies contributes 25% of medicines that is used in UK. India accounts for about 10% of the world's

production drugs by volume and 1.5% by value. Pharmaceutical export from India stood at US \$19.13 billion in 2018-19 and reached US \$13.69 billion till January 2020.²

EXPOSURE OF INDIAN PHARMACEUTICAL DEPENDENCY ON CHINA DURING COVID-19

As in the early era of 1991, a very few Indian pharmaceutical industries were reliant on Chinese imports and the import only account 0.3% of Indian bulk drugs import. But with the globalization, the Indian pharmaceutical companies and large-scale formulation manufacturing have started active pharmaceutical ingredient's (APIs) procurement from China and around the world due to the low cost of production of API in these

countries.³ During this uncertainty period, the concerns have been aggravated by the fact that COVID-19 struck China first, which is one of the global leaders in producing and exporting of APIs by volume.⁵ A significant number of pharmaceutical companies in India procure more than 70% of APIs for their finished drug formulation from China.

The majority of pharmaceutical ingredients production units in China are concentrated in Hubei province under which 30 to 40 units of basic chemicals, API and Intermediates are kept supplying the products to India. For some specific APIs like azithromycin, cephalosporin and penicillin the India's dependence on China is as high as 80 to 90%. According to (Pharmexcil report, 2019), India imported 17,400 crore INR worth of APIs from China.³

METHOD OF RESEARCH

The present paper analyzed the operational and technical challenges arises due to COVID-19 pandemic for pharma emerging markets and government initiatives to support pharmaceutical industry through a review of related published surveys during COVID-19. Further detail literature was also search to find out the macro and micro environmental factor that influence directly or indirectly to pharmaceutical industry.

PRE AND POST- COVID-19 PANDEMIC IMPACT ON INDIAN AND GLOBAL PHARMACEUTICAL INDUSTRY

Before the COVID-19 pandemic, it was forecasted that global pharmaceutical market would grow by 4-5% CAGR, reaching \$1.5 trillion and the overall value of drugs and medicine exports will increase by an average 5.8% for all exporting countries, which is of US \$371.3 billion. Indian pharmaceutical sector is also growing with the compound annual growth rate of more than 15%, which contribute a significant role in generic drugs.⁶

But after COVID-19 epidemic, the scenario of the pharmaceutical sector in developing countries may drastically change. It is predicted that the global pharmaceutical growth may lies in between 3% to 3.5% CAGR due to many factors like global recession, high currency volatility, diversification of fund by global organization, changes in drug regulatory policy, due to interrupted supply of API from export countries and ban of many drug formulations, and hand sanitizer, PPE, testing kits and respirators to other countries. These factors might propel the following changes in the pharmaceutical market of developing countries, as mentioned below:

Price of raw material and finished pharmaceuticals

With the lockdown of largest pharmaceutical suppliers like China, India and other developing countries during COVID-19 pandemic, there are chances of a sudden hike in the price of pharmaceutical raw material and finished

formulations. According to FDA report 2018, 13% of the brand and generic drug manufacturers are based out of China, whereas 31% of pharmaceutical ingredients and 24% of finished pharmaceuticals were imported from India. As an example, the cost of Paracetamol bulk drug in India has gone up to 400-450 INR per Kilogram from Rupees 250- 300 per kilogram. It is also reported that the price of vitamins and penicillin have increased by 40 to 50% in the Indian market. If the current situation remains continuously for a long time, the price of essential medicines might rise in India as well as in other developing countries.

Impact on essential drugs (generic drugs) supply chain system

Many developing countries include generic medicines under the national list of essential medicine (NLEM) as they are easily accessible and affordable to the public. The profit margin of these drugs is very marginal, and the supply chain is also lean. Many developing countries import API and finished formulation drugs from India and China market. The API manufactured from a single plant unit with limited batch production may hold very little inventory, and this may result in stock out or medicine shortages lasting from 14 months or even more than two years.¹⁵

The present situation caused by COVID-19 pandemic might cause a shortage of medicines and increase in demand of certain drugs like Hydroxychloroquine, Chloroquine and antiretroviral drugs like lopinavir and ritonavir, which are most talked about drugs during the pandemic time.

It is stated by some Indian pharma companies that for now as companies have stocks at least for the next five months, which may prevent sudden stock-outs or shortages of essential medicines. Indian pharma companies like Zydus Cadila, IPCA laboratories and Intas pharma has ramped up its production of hydroxychloroquine tablet by nearly 10 times to 30 metric tons which is equivalent to approximately 15 crore tablets of 200 mg per month.¹²

Intellectual property right and access to medicines in developing countries

International law requires that the countries across the globe should adopt minimum standards of intellectual property protection, while allows them to adopt measures to protect public health and to promote the public interest. IPRs have had a significant impact on global access to sustainable availability and access to affordable, quality, safe and efficacious essential medicines and diagnostics. Particularly, intellectual property law has played an increasing role in determining how medicines are developed, and how they can be accessed.

Drug development on a monopoly-based policy may fail the world. The open science and research practices for

COVID-19 treatment should be supported by all country governments. These efforts should be aligned with innovation and timely access. Accessibility and affordability of COVID-19 treatment should be an integral part of the entire research and development (R&D) and manufacturing processes across the globe.^{10,12}

Drug regulatory policy

The regulatory authority may allow some relaxations to meet out the demand for medicine during the lockdown period. As the review process of the generic drug by the regulatory authority is lengthy, but the demand for drugs and shortages of drugs may also force to make drug marketing authorization a fast track approval. The government of India allows import of drugs which may cross more than 40% of their self-life or having few months to the expiry date to meet the demand during COVID-19 pandemic. The government of developing countries take strict action regarding the export of the essential drugs and medical devices which are required during the COVID-19 pandemic. The India pharmaceutical companies, which are involved in manufacturing of scheduled formulations under the Drugs Prices Control Order (DPCO 2013), must carefully monitor their output levels of production and if any pharma manufacturer needs to discontinue manufacture of any scheduled formulations due to the unavailability of APIs, than the company must notify to the

central government in accordance with DPCO 2013 provisions so that central government could take other preventive measures to safeguard the public health demand for that medicine.^{8,15}

Trends in the clinical trial market

The global clinical trials market size has been estimated at USD 18.4 billion in 2019. It is projected to reach USD 26.9 billion by 2024 at a CAGR of 7.83% during the forecast period from 2019 to 2024 (Grand view research, 2020). Globally more than 8000 plus Investigational New Drug Application (IND) filled to various regulatory bodies by the research and pharmaceutical organization for research and development of COVID-19 vaccines, drugs, and antibodies treatment. The EU clinical trials register currently displays 36915 clinical trials with a Eudra CT protocol out of which 6088 are clinical trials conducted with subjects less than 18-years-old. USFDA encourages recovered patients to donate plasma for development of blood-related therapies. USFDA also issues recommendations for investigational COVID-19 convalescent plasma. Indian Council of Medical Research (ICMR) initiated two clinical trials of plasma therapy for the treatment of critically ill COVID-19 patients that is one for convalescent plasma therapy and another for plasma exchange therapy.⁸

Table 1: Current research activities by pharmaceutical and research organization against COVID-19 disease.

Research type	Target	Clinical phase	Current status and plans	Timeline
Treatment	Remdesivir	Phase III	Remdesivir is now being tested in five COVID-19 clinical trials that have been set up at breakneck speed.	CT results are expected in April 2020
Treatment+ vaccine	Plaquenil	Pre-clinical	Conduct additional clinical trials (CTs) and supply millions of doses of an existing anti-malaria product new mRNA	NA
Treatment+ vaccine	New mRNA vaccine	Pre-clinical	Co-development of a new product clinical testing in humans. Research performs on strands of mRNA to spur the production of protective antibodies.	CTs are planned to be started in April 2020
Vaccine	COVID-19 vaccine	Pre-clinical	Research is done on the same vaccine platform which is earlier used to develop ebola vaccine	R&D in January 2020 & CT to be started by the end of November 2020.
Treatment	Lopinavir/ritonavir combination	Phase III	The research organization is collaborating with select health authorities and institutions globally to determine antiviral activity as well as efficacy and safety of lopinavir/ritonavir against COVID-19	NA
Vaccine	Lopinavir/ritonavir combination	Phase II	A platform to newnext-generation sequencing workflows focused in microbiology and infectious disease, including for the novel coronavirus	Started in March 2020

Continued.

Research type	Target	Clinical phase	Current status and plans	Timeline
Treatment	Monoclonal antibody therapy	Pre-clinical	To select the top 2 antibodies for a cocktail therapy, which can either be administered to the people at risk before exposure to infection as a vaccine or as treatment	Potential to enter human CT by early summer 2020
Treatment	Polyclonal antibody therapy	Pre-clinical	Collaboration with several health and regulatory agencies and health care partners across the globe on its TAK-888. The company is trying to access to source plasma from people who have successfully recovered from COVID-19	Started in March 2020

European Pharmaceutical Review (2020).

The surge of counterfeit medicines in developing countries

WHO recently has warned the developing countries in concern to growing numbers of fake drugs linked to coronavirus treatment. In the present pandemic situation around the world with the growing gaps in the pharmaceutical supply chain system, the counterfeit medicines are exploiting more in low and middle-income countries. The majority of people in these countries are hoarding of necessary drugs at home, and due to lockdown in countries of largest pharmaceutical suppliers like India and China, the supply and demand are moving towards the danger zone, which also soaring the counterfeit drugs market.

During COVID-19 pandemic Interpol global pharmaceutical crime-fighting unit made 121 arrests across 90 countries resulting in the seizure of dangerous pharmaceuticals worth over \$14 million.

The government authorities have confiscated thousands of counterfeit face masks and fake medicines in different countries. Such drugs make a false claim to be able to cure coronavirus infection.¹⁶

WHO report states that falsified medicines trade, which includes contaminated medicines, drugs containing the wrong or no active ingredient, or maybe out-of-date drugs, is having a worth of \$30 billion in low and middle-income countries.

The cases of self-medication and irrational use of medicines are on rises during COVID-19 epidemic. Several recently published news reports have referred to the issues of potency and therapeutic gain against coronavirus infection, of drugs like chloroquine and hydroxychloroquine.

Such drugs may lead to side effects, if used as self-medication.

GOVERNMENT ACTION AND PHARMACEUTICAL PREPAREDNESS AGAINST COVID-19 PANDEMIC

After the corona epidemic, the governments of India has set up a task force to review the API sector in India.¹³ The several critical representatives of the pharmaceutical industry and NITI Aayog raised their concern regarding fostering the approval of pharmaceutical infrastructure developments, clearance from the environment ministry and providing tax exemptions and subsidies for the development and promotions of the pharmaceutical industry hubs (Figure 1).

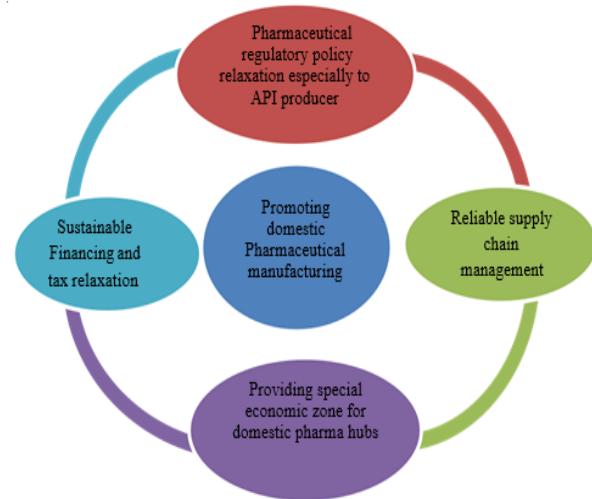


Figure 1: Proposed strategies for promoting Indian pharmaceutical API and medical device sector.

The pharmaceutical authority and government agency are working together for removing technical and financial barriers and spur the pharmaceutical industry into immediate action for ramping up APIs production to decrease the dependency of the pharmaceutical industry on China. In this view recently the government of India has taken applaudable steps by proposing incentive package of 13,760 crore INR for the promotion of domestic pharmaceutical manufacturing. This package including

starting material, drug intermediates, APIs and medical devices. In addition to incentives, the government also announces three bulk drug parks and four medical device parks for fostering domestic production.¹⁴

Pharmaceutical management in developing countries can be strengthened with a global coordinated plan for coordinated production, equitable distribution and the surveillance of the quality of the tests kits, medicines and vaccines. The pharmaceutical regulatory framework should be harmonized and well functioned among all developing countries. The access to essential medicine during a national health emergency in low and middle-income countries can be managed with a rational selection of drugs at an affordable price with sustainable financing and reliable health supply systems. More healthcare professionals and people should be aware and trained about the judicious use of drugs during the national pandemic. People should be well educated regarding harm of self-medication at home.

CONCLUSION

COVID-19 epidemic may not spare any nation or people of any faith or followers of any custom. If the epidemic goes unattended in one country, it will accelerate beyond that country's borders and will spread throughout the globe. Nationalistic responses to COVID-19 are ineffective. Developed and developing countries must work together to ramp up the production of all medical countermeasures, from PPEs and ventilators to tests, treatments and vaccines, and ensure that everyone receives the medical attention they need. The COVID-19 pandemic might impact pharmaceutical industries in many different ways in developing countries, and that can only be restricted by moving pharmaceuticals, health agencies and governments to share medical technology and invest in enhancing public manufacturing capacity and promote access of drugs and equipment to all. In this pandemic situation solidarity and global cooperation among pharmaceutical companies, research organization and government agencies can accelerate the innovation, quickly scale-up production and mitigate shortages and supply chain vulnerability. Medical tools must be manufactured for the public in robust supply to meet the unprecedented global need and promptly distributed across borders.

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