Indian drug companies think the current coronavirus crisis could be a boost for India’s bulk drug manufacturing companies and an opportunity to again become a preferred active pharmaceutical ingredient (API) supplier of pharma products for the world.

India currently imports around 90% of the APIs from China. However, following API constraints due to the situation in China, the Indian government has taken measures to bolster domestic capabilities and has set aside $1.2bn for the pharma sector to shift the country away from its reliance on APIs from China.

The situation started deteriorating from the start of 2020. As the pandemic played out in China, the reduced flow of API imports and bulk drugs severely disrupted India’s $39bn pharmaceutical drug production industry. Vast swathes of the Chinese economy were shut down before Covid-19 became a global pandemic, exposing India – the world’s single-largest exporter of generic drugs – to face up to the country’s dependence on Chinese imports.

Imported raw ingredients and APIs are used to manufacture key medicines such as paracetamol, metformin, ofloxacin, metronidazole, ampicillin and amoxicillin. As consignments from China slumped, drug prices shot up in India. Paracetamol doubled in price, while nimesulide tripled in price. Prices for azithromycin, used for bacterial infections, and montelukast, for treatment of respiratory infections, also shot up by about 30%.

As the outbreak in China exposed faults in the antibiotics pipeline, the Indian government got down to the task of identifying 53 key starting materials and APIs. A task force to look into boosting output on a priority basis was also initiated.

Apart from the $1.2bn boost to set up three drug manufacturing hubs, the government has also decided to take on the onerous task of reviving loss-making state-owned bulk drug-makers, namely Hindustan Antibiotics and Indian Drugs and Pharmaceuticals, to ensure affordable medicines. Over the past decade, seven or eight manufacturing plants have shut-down due to the ‘cheaper alternatives’ from China. These plants used to produce 20 ingredients such as penicillin G, erythromycin, rifamycin, tetracycline, citric acid and vitamin B12.

In the 1980s, India was one of the world’s largest producers of semi-synthetic penicillin. China strategically reduced the cost of penicillin G by over 80%, leading to the closure of some of the India’s largest bulk pharma plants. The government has now decided to look at upgrading and restarting some of the plants, especially since the Department of Pharmaceuticals highlighted how the disruption had increased prices of some basic drugs and antibiotics by 70%.

In a country where 75% of the out-of-pocket expenditure for healthcare by people is for medicines, this could deeply impact the healthcare choices available to the poor.

Meanwhile, the Federation of Indian Chambers of Commerce and Industry has also recommended incentivising drug manufacturers. And since India has the technology for fermentation-based APIs, key starting materials and intermediates, the government is also working on new policy to strengthen the Indian API market.

In a pre-Covid era, India used to rely on bulk ingredients from China to manufacture a fifth of the global supplies of off-patent drugs. But that could be set to change in the coming months.

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**Better batteries**

**MARIA BURKE**

A fundamental physics technique shows promise in energy materials research. It allows researchers to map the chemical states of battery electrodes to better understand battery performance.

Wanli Yang, at the US Department of Energy’s Lawrence Berkeley National Laboratory’s Advanced Light Source facility, has adapted an X-ray technique known as mRIXS (resonant inelastic X-ray scattering) and named it high-efficiency mRIXS. ‘Scientists were trying to see inside a battery material – not only at the surface, but also in the bulk – to learn about its oxygen atoms and metal states,’ Yang says. ‘Most conventional techniques lack either the depth of probe or the chemical sensitivity that could be offered by mRIXS.’

In the technique, an X-ray beam scans a sample of electrode. It maps samples by measuring the chemical states of elements at a specific point in the battery’s charge or discharge cycle, giving information on whether, and how fully, battery materials are stably gaining and losing electrons and ions. mRIXS takes three hours to complete a map scan, compared with days with other techniques (Science Adv., doi: 10.1126/sciadv.aaw3871).

‘The uniqueness of the system is not only the data collection time, but its ability to look at unconventional chemical states that typically are not very stable under X-rays,’ comments Yang. Changes in oxygen states – as a result of oxygen redux – have been found to hamper battery performance in studies of lithium-rich electrodes. Changes of the oxygen states could make the battery unsafe and also trigger side-reactions if the process isn’t reversible, he explains.

Yang says mRIXS can detect whether the oxygen redox states are reversible and also metal states. This makes it useful for studying high-voltage, high-capacity battery materials that are of growing interest.

The technique has been integral to several battery studies published in recent months, Yang adds. ‘The demand is increasing extremely fast and [we are] in the process of developing new RIXS systems with even higher throughput due to this demonstrated capacity and increasing demand. The community was in dire need of such a tool.’
Japanese drug for Covid

In mid-March 2020, Chinese minister Xinmin Zhang reported that Japanese drug favipiravir was effective in treating Covid-19 patients. Administered under the brand name Avigan, the drug was developed by Toyama Chemical, now owned by Fujifilm.

According to Zhang, who leads the China National Center for Biotechnology Development, patients taking favipiravir in a clinical trial involving 80 patients at the Third People’s Hospital of Shenzhen tested negative after an average of four days, compared with 11 days in the control group. Another clinical trial with 240 patients at a Wuhan hospital showed that 8.2% of patients treated with favipiravir needed respiratory aids, compared with 17.1% of patients in the control group.

‘The drug is very safe and clearly effective,’ Zhang said at a Beijing press conference.

Fujifilm shares jumped 15.4% the next day. Three days later, Indonesian president Joko Widodo said at a televised press briefing they have ordered 5000 doses of favipiravir. The Japanese government has since ordered 2m tablets, and the drug is undergoing Phase 3 trials there. China’s Zhejiang Hisun Pharmaceutical is set to produce a generic version. The drug also entered Phase 2 trials in the US.

Favipiravir was developed for anti-influenza activity in the 1990s. It is a broad-spectrum inhibitor of RNA polymerase, preventing a virus’s RNA from replicating itself inside infected host cells. According to a 2017 study led by Fujifilm researcher Yousuke Furuta, the drug could be effective against a range of RNA viruses, including Zaire Ebola virus, rabies virus and flaviviruses like West Nile and Zika viruses. In 2016, the Japanese government provided favipiravir to Guinea as emergency aid for the Ebola outbreak.

However, the same study noted that ‘favipiravir has a risk for teratogenicity and embryotoxicity.’ In 2014, the Japanese government approved favipiravir for novel strains of influenza, to be deployed only if the government decides it necessary against new or re-emerging influenza viruses. The drug remains contraindicated for pregnant women, who are not included in the Japanese Phase 3 trials.

South Korea has announced it will rule out the use of favipiravir to treat the novel coronavirus after its team of infectious diseases experts concluded there was inadequate data supporting its efficacy and the potential for ‘serious side effects,’ according to Yonhap News Agency. The neighbouring nation instead is conducting trials of remdesivir, another RNA polymerase inhibitor, from US pharmaceutical giant Gilead Sciences.

Furuta declined to comment as the company is currently conducting clinical trials. Fujifilm has since announced it will ramp production to more than double, compared with the beginning of March.

Reinfection or reactivation

In April 2020, reports surfaced in China and South Korea that some patients who recovered from Covid-19 have tested positive for the SARS-CoV-2 virus responsible for the disease again.

Most countries require Covid-19 patients test negative at least twice consecutively for the virus before release from quarantine. The patients who tested positive again had all tested negative for the virus during their recovery. It is unclear whether these patients continue to be a risk for transmission.

By 26 April, there were 263 such patients in South Korea, some 3% of recovered patients, according to Yonhap News Agency. Precise figures are not available from China, but Reuters reports there are at least ‘dozens’ of cases.

The Korea Centres for Disease Control and Prevention examined 25 such patients and found protective antibodies against the SARS-CoV-2 virus in all. However, 12 also tested positive for the virus.

Post-recovery development of immunity against the virus has thus been cast in doubt. ‘There is currently no evidence that people who have recovered from Covid-19 and have antibodies are protected from a second infection,’ the World Health Organisation (WHO) stated on 24 April.

The WHO also cautioned against using the presence of antibodies to the SARS-CoV-2 virus as the basis for immunity passports. ‘People who assume that they are immune to a second infection … may ignore public health advice.’

Researchers are still investigating why the virus appeared to re-emerge in recovered patients. South Korean health officials suggested the virus could have ‘reactivated’ – like how chickenpox virus can lie dormant and become active again later to cause shingles.

Another possibility is reinfection after full recovery, although most cases tested positive a second time shortly after recovery – some while still in quarantine. ‘I’m sure they were not reinfected,’ Zhao Yan, a doctor at Zhongnan Hospital in Wuhan told Reuters of the cases he has seen.

An early February study from the Third People’s Hospital of Shenzhen suggested faulty tests could have been to blame. Specifically, tests that produced false negatives and later detected RNA debris from dead virus.

More recently, researchers in China discovered RNA from the SARS-CoV-2 virus in the lungs of a 78-year-old Covid-19 patient who died mid-February of unexpected cardiac arrest. Cell Res., doi: 10.1038/s41422-020-0318-5. Four days before her death, the patient had tested negative for the virus for three consecutive days and was ready for discharge. Because of their findings, the Chongqing researchers suggested that the usual nasal swab test may be insufficient.
Air quality boost for India

A. NAIR

Air pollution kills 1.25m people in India every year. India’s capital New Delhi has the worst air pollution of any capital city. However, air pollution has dropped dramatically as a result of lockdown to control coronavirus. And the resulting clear air could aid the battle against Covid-19, as air pollution makes people more vulnerable to lung disease.

As the countrywide lockdown completed one month on 25 April, NASA satellite sensors observed aerosol levels at a 20-year low for this time of the year in parts of northern India. Delhi, which has been trying to cope with the alarming levels of air pollution by installing smog towers and water sprinklers, is suddenly pollution free.

Ever since the 21-day lockdown began on 25 March, 2020 the 36 functioning air monitoring stations in Delhi have been reporting a drastic drop in pollution. In November 2019, air pollution levels in Delhi had soared to hazardous levels, forcing the local government to declare a public health emergency, shutting down schools and cancelling flights. Some reports have even suggested breathing Delhi’s air for one day has the health impact of smoking at least 25 cigarettes/day.

All of that appears to have been turned on its head.

As industrial units temporarily downed shutters and most vehicles kept off the road immediately after the lockdown announcement, data from Air Quality Index (AQI) website (aqi.in) showed dramatic air quality improvements around Delhi within just three days. AQI is a measure based on concentrations of particulate matter (PM), ozone, nitrogen dioxide (NO2), sulfur dioxide (SO2) and carbon monoxide emissions.

Delhi recorded its best-ever AQI score of 45 on 28 March, after a spell of rain and four days after the lockdown commenced. In Anand Vihar, one of the most polluted areas of New Delhi, the recorded AQI was 65 on 22 April at 5pm – compared with more than 400 on several occasions in April 2019. PM2.5 refers to PM having diameter less than 2.5 micrometers, which can enter the lungs and even the bloodstream.

Apart from Delhi, several major cities like Mumbai, Kolkata, Bengaluru and Chennai also witnessed significant drops in the level of major air pollutants. AQI data from the second week of March till April 6 showed Delhi registering a 62% drop in PM2.5 levels and a 50% drop in NOx. Ahmedabad recorded a 57% drop in PM2.5 levels and a 32% drop in NOx.

Mumbai, on the other hand, recorded a 45% drop in PM2.5 levels during the same three-week period and a 60% drop in NOx, while Pune recorded a 31% drop in PM2.5 levels and a 62% drop in NOx.

India’s Central Pollution Control Board (CPCB), too, reported an improvement in air quality across the country. The lockdown improved the AQI to satisfactory levels in nearly 90% of the 103 cities monitored by the CPCB, according to data on the environmental agency’s website.

The CPCB monitored 115 cities between March 16 and April 15. A 47% reduction in PM2.5 levels was observed mainly due to restrictions on transport and industrial operations. The two major sources of benzene emissions: CPCB data showed the concentration of PM, NOx and SO2 emissions reduced significantly. Overall, NOx levels dropped 71%.

CPCB, the apex pollution control body, said significant reduction in PM2.5, PM10 and NO2 levels were observed across the country. Several cities registered drops of over 50% in NOx levels, with Kanpur registering a decline of 72%.

Overall, a 66% reduction in PM2.5 and 50% reduction in PM10 concentration was observed during the lockdown period, both from combustion and industrial sources.

Scientists expect aerosol levels to increase slightly, however, in the coming weeks in parts of India as seasonal dust storms commence. Air pollution also is expected to rise with rising temperatures. For the next few days, temperature readings will frequently touch 46°C.

Although scientists have seized the lockdown window to understand background levels of air pollutants, environmentalists believe the reduced pollution levels should act as a wake-up call for the government.

Jyoti Lavakare, Co-Founder, Care for Air NGO, said the low AQI and the blue skies proves ‘beyond doubt that a lot of the polluted air was anthropomorphic, that is, man-made. Obviously, slowing down the economy to such an extent is not the ideal way to bring down air pollution, but at least it proves that it can be done. We can achieve the same outcome by doing this mindfully, using technology and low-emission alternatives’.

Ravina Kohli, environmentalist and part of the #MyRightToBreathe campaign said: ‘For the first time, our present generation will discover the critical need for a focus on public health and quality of air we breathe.’

As India focuses on getting factories and businesses going again, the virus may be an opportunity for climate activists to propose their transformative agenda toward a green, clean economy.
14 May
Briefing – Industrial Decarbonisation Research and Innovation Centre (IDRIC)
Start: 11:00
Organised by SCI’s Energy Group
Free Online Webinar
+44 (020) 7598 1561
Conferences@soci.org

14 May
New Permit to Work Training Course
New and extended course for anyone requiring to increase their understanding of permit-to-work systems, including those who issue permits.
Leeds, UK
Cia.org.uk

19-21 May
Vaccine Bioprocess Development and Commercialisation
Understand the challenges of creating a vaccine process and explore risk-based decision making for bioprocess analytics.
London, UK
https://ucl.ac.uk/biochemical-engineering/study

19-21 May
UTECH North America 2020
Polyurethanes trade show covering all end markets and sections of the supply chain – from flexible, rigid and spray foams, through to coatings, elastomers and sealants.
Chicago, Illinois, US
Utech-north-america.com

21 May
Shaping Biotech’s Future
Focus on the specific needs of the Biotech and Emerging Pharma segments and their partners; a forum to discuss the major challenges impacting the sector.
London, UK
LifeSciencentrales.com/bio-integrates-2020/

24 June
Paul Hodges – Chemistry and Chemicals in the UK
Reg: TBC
Organised by SCI
Free Online Webinar
+44 (020) 7598 1561
Conferences@soci.org

3 September
Irish Polymers and Materials Conference 2020: Polymers and the Environment
Start: 18:30 Reg: 18:00
Organised by SCI
SCI, UK
+44 (020) 7598 1561
Conferences@soci.org

10 October
Highlights in Medicinal Chemistry IV
Start: TBC
Organised by SCI’s Fine Chemicals Group
SCI, UK
+44 (020) 7598 1561
Conferences@soci.org

13 October
Automated Intelligent Chemistry
Start: TBC
Organised by SCI’s Young Chemists’ Panel
SCI, UK
+44 (020) 7598 1561
Conferences@soci.org

20 October
Pavement Surfacing Materials – What’s new?
Start: TBC
Organised by SCI’s Construction Materials Group
SCI, UK
+44 (020) 7598 1561
Conferences@soci.org

22 October
Future opportunities for CO₂: the chemistry of carbon dioxide and its role in decarbonisation
Start: TBC
Organised by SCI’s Energy Group
SCI, UK
+44 (020) 7598 1561
Conferences@soci.org

28 October
Exploding Black Holes and Gravitational Waves – Prof Carole Mundell
Start: 18:30 Reg: 18:00
Organised by SCI
SCI, UK
+44 (020) 7598 1561
Conferences@soci.org

2 November
27th SCI Young Chemist in Industry 2020
Start: TBC
Organised by SCI’s Young Chemists’ Panel
Signature Discovery, Hucclecfield, UK
+44 (020) 7598 1561
Conferences@soci.org

10 November
SCI-RSC Challenges in Catalysis VII
Start: TBC
Organised by SCI’s Fine Chemicals group and RSC’s Applied Catalysis Group
RSC, UK
+44 (020) 7598 1561
Conferences@soci.org

16-17 November
3rd SCI-RSC Symposium on Antimicrobial Drug Discovery
Start: TBC
Organised by SCI’s Fine Chemicals Group and RSC’s Biological and Medicinal Chemistry Sector
SCI, UK
+44 (020) 7598 1561
Conferences@soci.org

25 November
Predatory Bacteria – Prof Liz Sackett
Start: 18:30 Reg: 18:00
Organised by SCI
SCI, UK
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