

2020

Clinical Landscape Report on Ivermectin

Potential candidate for Prophylaxis & treatment



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Preface

It's been months and still the whole world is trying desperately to invent a new drug or to repurpose an old one. In this scenario, the key to drug discovery for this deadly virus is intelligence on all such treatments and vaccines. While it will take 12-18 months for vaccines to come, the best bet we have to save the world is to find an **existing drug that has a proven safety profile** and for treating COVID-19 patients.

The COVID-19 pandemics has fueled research efforts towards repurposing existing drugs as possible antiviral agents, whereby the therapeutic strategies have been largely based on pre-existing data for the preceding coronavirus outbreaks TORS and MERS1-3. The drug regulatory agencies, health authorities, key opinion leaders and policy decision makers have been significantly strained by the dilemma of **evidence-based medicine and good clinical practice** versus the **prompt need for safe and effective treatment**. Unfortunately, we have been witnessing huge public and political pressure for legitimization of drug-repurposing and off-label use worldwide, which nonetheless could be regarded as an acceptable compromise, pending the emergency of the current situation, but only in case of drugs with well-defined safety profiles and at least some clinical evidence in COVID-19.

The report presents one such existing drug **Ivermectin**, as a potential preventive medication to reduce viral load of COVID-19. It is **also known as 'wonder drug'** like Penicillin and Aspirin, is an **FDA-approved** anti-parasitic previously known to have broad-spectrum anti-viral activity in vitro and most importantly is an **inhibitor of the causative virus (SARS-CoV-2)**. The only way to **break the chain and bring back the economy on track** is to find an already proven FDA approved drug which has been successfully mass administered in past with exceptional safety profile and most importantly is affordable for Indians unlike super expensive drugs, like **Remdesivir, which will cost approximately INR 50,000 for a 5 days' course** (even for a generic version). One example of its efficacy is from the results of trials. Its use has shown a **~5000-fold decrease in the viral load within 48 hours**. Ivermectin has also **reduced mortality rates** in hospitalized COVID-19 Patients in a Cohort Clinical Study Conducted in South Florida.

The proposed generic drug reduces efforts and costs for developing a new vaccine. This report covers the major research conducted globally for determining efficacy of Ivermectin for COVID patients. The report provides exhaustive details on safety profile of, its adverse events recorded in history, its past clinical trial records and combinations, record of brand names under which it is sold in India, pros and cons on the use of Ivermectin, etc.

Perhaps more than any other drug, **Ivermectin is a drug for the world's poor**. For most of this century, some 250 million people have been taking it annually to combat two of the world's most devastating, disfiguring, debilitating and stigma-inducing diseases, Onchocerciasis and Lymphatic filariasis. Most of the recipients live in remote, rural, desperately under-resourced communities in developing countries and have virtually no access to even the most rudimentary



of medical interventions. Moreover, all the treatments have been made available free of charge thanks to the unprecedented drug donation program.

The said 45-year-old drug has been described in detail in the report. This helps to compare Ivermectin against the drugs available currently for the treatment of COVID. With WHO predicting the global number to touch 10 million soon, we need a drug that has **high efficacy and low side effects**. The number of researches across the globe, the history of drugs, lack of side effects and its economic availability are evident and thus there is an urgent need to push forward for a fast tracked clinical trial. It will be a matter of pride for India, if we become the first country to conclude the accelerated clinical trials with a positive outcome nationwide (or at least in the red zones where infection is increasing beyond manageable limit) of this 50 years old drug with very good safety profile.



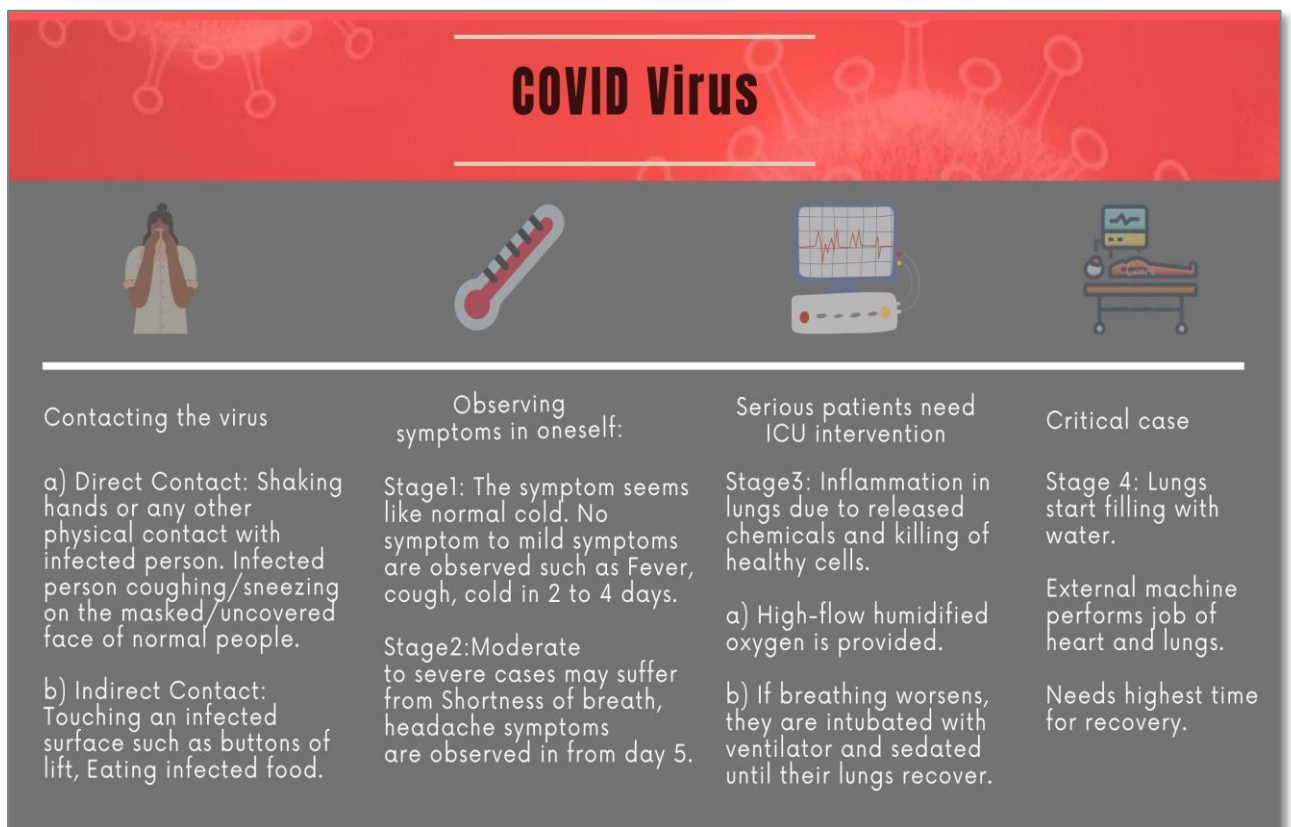
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About COVID-19

The coronavirus COVID-19 pandemic has caused a global health crisis of our time and the greatest challenge we have faced since World War II. Since its emergence in China late last year, the virus has spread to every continent except Antarctica. Cases are rising daily in all the affected countries and forcing them to go into lockdown which has impacted the economies of each country and it is taking all the countries back by 5 to 7 years. Hence COVID-19 is much more than a health crisis. COVID-19 is a highly contagious SARS-CoV-2 coronavirus that is rapidly spreading through both our most vulnerable and healthy population.

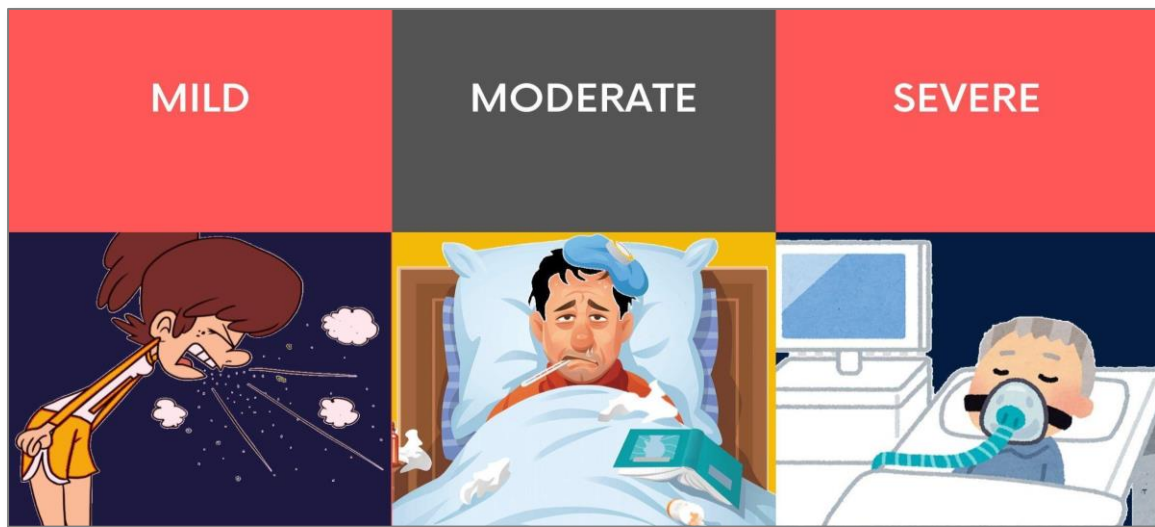


A. COVID-19 Timeline

With over a few lakh cases in the country and doubling rate at over 15 days, India requires urgent control. This is possible only through use of proper drugs and vaccines. The available drugs for corona have been divided into three sections, based on the stage at which they are in use. To achieve the aim of flattening the curve, it is important to reduce the number of patients from entering the moderate stage from the mild stage. **Such drugs that are effective in mild stages can help break the chain.**

The virus spreads takes place due to the viral load of an infected person. Virus gets inside the body of a healthy person and starts affecting the lungs. New virus starts growing at the site and starts damaging cells by killing it. Immune system recognizes an intruder and signals the body

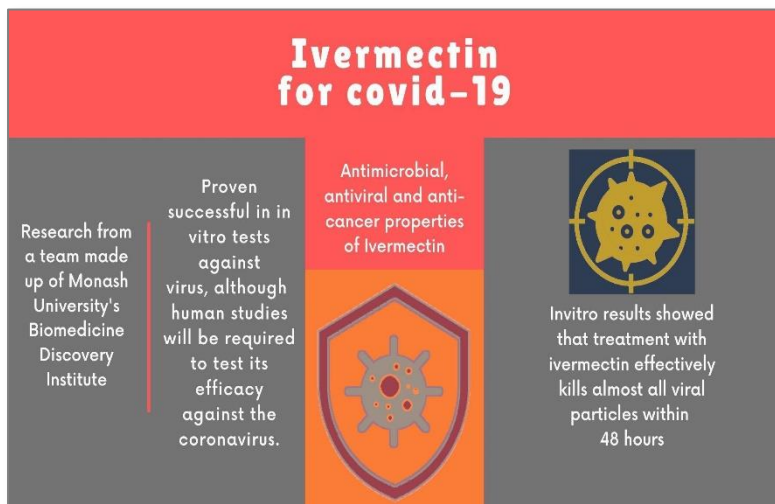
by releasing chemicals. At this point of time, the person needs to quarantine to arrest further spread. If the condition of the patient deteriorates further he will need ICU care, ventilation and in extreme cases even life support.



B. Why is Ivermectin a treatment candidate for COVID-19?

The latest **research from a team at Monash University's Biomedicine Discovery Institute (BDI)** and the Peter Doherty Institute of Infection and Immunity indicated that Ivermectin could form the basis of a Covid-19 vaccine given that it has proven successful in in vitro tests against other viruses, although human studies will be required to test its efficacy against the coronavirus.

Ivermectin has many possible benefits including its antimicrobial, antiviral and anti-cancer



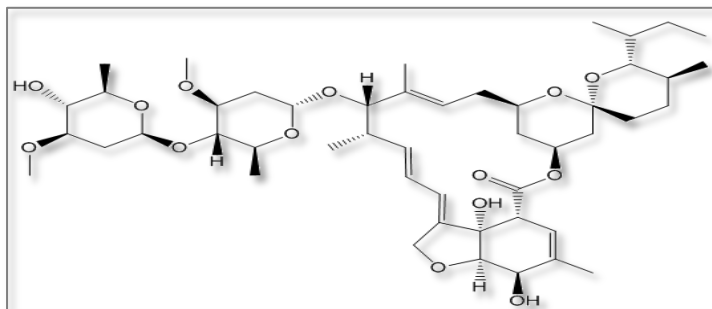
properties like the product of curiosity. It is highly successful against many, including certain viruses, micro-organisms. In this comprehensive systematic review, antiviral effects of Ivermectin are summarized including in vitro and in vivo studies over the past 50 years. [1]

In a recent in vitro study, the **Vero/hSLAM cells infected with the SARS-CoV-2 or COVID-19 virus were exposed to 5 μ M**

Ivermectin in 48 h, and a 5000-fold reduction in viral RNA was found. The results showed that treatment with Ivermectin effectively **kills almost all viral particles within 48 hours**. The study has been the first one to assess Ivermectin's antiviral effect on the body. [2]

Later the potential of the drug was acknowledged and a full-fledged study was proposed on the drug. Also, the fact that Ivermectin has previously been effective against HIV, Dengue, Simian Virus, Zika Virus, Influenza all of these being RNA Virus, the chances have been predicted for Ivermectin to be a cure for covid-19s.

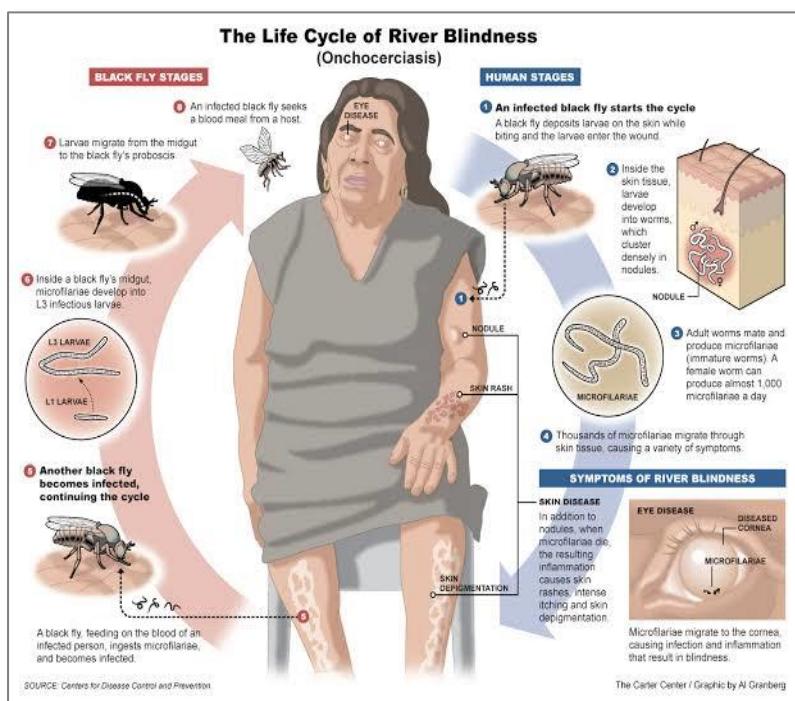
About Ivermectin



Ivermectin is a broad spectrum antiparasitic agent that is also referred to as **‘wonder drug’**[3]. It falls under the Ivermectin family of medications which includes drugs and pesticides that are used in the treatment of parasitic worms and insect pests. Ivermectin is a part of the World Health Organization’s list

of essential medicines [4] under the ‘Antifilarials’ category.

A. Onchocerciasis Disease



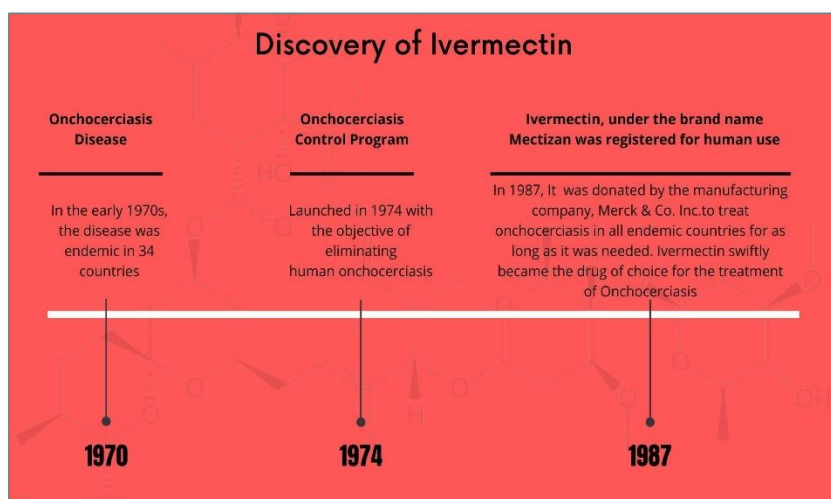
The origins of Ivermectin as a human drug are inextricably linked with Onchocerciasis, also known as River Blindness. It is caused by infection caused by *Onchocerca volvulus* worms. After mating, female worms can release up to 1000 microfilariae a day for some 10–14 years. These move through the body, and when they die they cause a variety of conditions, including skin rashes, lesions, intense itching, oedema and skin depigmentation. These **Microfilariae also invade the**

eye, causing visual impairment and loss of vision. Onchocerciasis is the second leading cause of blindness caused by an infectious disease. The disease causes visual damage for some 1–2 million people, around half of whom become blind.

In the early 1970s, the disease was endemic in 34 countries: 27 in Africa; 6 in the Americas; and 1 in the Arabian Peninsula. The World Health Organization (WHO) later estimated that 17.7 million people were infected worldwide, of whom some 270,000 were blind, and another 500,000 severely visually disabled. [5]

B. Discovery of Ivermectin

The Onchocerciasis Control Programme was set up in 1974. At exactly this time, a specialized novel anthelmintic mouse screening model in Merck's research laboratories was identifying the avermectins in the microbial sample sent by the Kitasato Institute, of which Ivermectin would become the most successful derivative.



Ivermectin, under the brand name of "Mectizan" for human use was registered in 1987. It was donated by the manufacturing company, Merck & Co. Inc. to treat onchocerciasis in all endemic countries for as long as it was needed. It swiftly became the drug of choice for Onchocerciasis treatment due to its unique and potent microfilaricidal

effects, the **absence of severe side effects and its excellent safety.** [5]

Since the prodigious drug donation operation began, 1.5 billion treatments have been approved. Latest figures show that an estimated 186.6 million people worldwide are still in need of treatment, with over 112.7 million people being treated yearly, predominantly in Africa.



C. Pharmacokinetics and Pharmacodynamics of Ivermectin

The broad-spectrum antiparasitic agent **Ivermectin** has been very recently found to inhibit **SARS-CoV-2** in vitro and proposed as a candidate for drug repurposing in COVID-19. We analyze the in vitro antiviral activity end-points from the pharmacokinetic perspective. The available pharmacokinetic data from clinically relevant and excessive dosing studies indicate that the SARS-CoV2 inhibitory concentrations are not likely to be attainable in humans.^[6]

The causative agent of the current COVID-19 pandemic, SARS-CoV-2, is a single stranded positive sense RNA virus that is closely related to severe acute respiratory syndrome coronavirus (SARS-CoV). Studies on SARS-CoV proteins have revealed a potential role for IMP α / β 1 during infection in signal-dependent nucleocytoplasmic shuttling of the SARS-CoV Nucleocapsid protein (Rowland et al., 2005; Timani et al., 2005; Wulan et al., 2015), that may impact host cell division (Hiscox et al., 2001; Wurm et al., 2001). In addition, the SARS-CoV accessory protein ORF6 has been shown to antagonize the antiviral activity of the STAT1 transcription factor by sequestering IMP α / β 1 on the rough ER/Golgi membrane (Frieman et al., 2007). Taken together, these reports suggested that Ivermectin's nuclear transport inhibitory activity may be effective against SARS-CoV-2.

Ivermectin is a semisynthetic analogue of the natural product avermectin B1a, a lipophilic macrolide isolated from *Streptomyces avermitilis* developed as a crop management insecticide. Its mode of action on target species is by potentiating GABA-mediated neurotransmission and by binding to glutamate-gated Cl⁻ channels, found only in invertebrates. The drug induces tonic paralysis of the musculature of susceptible parasites, and eventually death. At the recommended doses, Ivermectin does not readily penetrate the CNS of mammals, where GABA functions as a neurotransmitter. Conversely, in healthy volunteers and infected patients the drug is usually well tolerated at the therapeutic dose ranges. A recent meta-analysis has shown that even larger doses (up to 800 μ g/kg) with a several years' period of follow-up could be well tolerated in patients with parasitic infections. The largest dose intensity with registered pharmacokinetic parameters in healthy subjects is 120 mg, corresponding to up to 2000 μ g/kg¹². As evident from the analyzed pharmacokinetic data both the clinically applied dosage schedules and the aforementioned excessive 120 mg dose yield blood levels at the nanogram/ml i.e. nanomolar range. These concentrations are orders of magnitude lower, as compared to the in vitro antiviral end-points, described in the study of Caly et al.¹¹. Table 2 summarizes the in vitro inhibitory concentrations, recalculated in ng/ml (based on a molecular weight of 875.1) to allow direct juxtaposition with the pharmacokinetic parameters in Table 1. Moreover, the in vitro data have been compared to the C_{max} values, obtained after 36 mg and 120 mg doses corresponding to dose intensities of up to 700 μ g/kg¹⁷ or 2000 μ g/kg¹² respectively, with calculation of the corresponding exposure ratios. The analyzed data show that at least at the clinically relevant dose ranges of Ivermectin the published in vitro inhibitory concentrations and especially the 5 μ mol/L level causing almost total disappearance of viral RNA are virtually not achievable with the heretofore known dosing regimens in humans. The 5 μ mol/L concentration is over 50 times higher than the levels obtainable after 700 μ g/kg¹⁷ and 17 times higher vs. the largest C_{max} found in the literature survey (247.8 ng/ml)¹². Moreover, the authors' claim for achieving viral inhibition with a single dose is inappropriate because practically the infected cells have been continuously exposed at concentrations that are virtually unattainable even with excessive dosing of the drug. With other words the



experimental design is based on clinically irrelevant drug levels with inhibitory concentrations whose targeting in a clinical trial seems doubtful at best. [7]

The plasma systemic exposures increase proportionally with doses between 6 and 120 mg. After single 12 mg doses of oral Ivermectin (tablet) in healthy volunteers, the mean peak plasma concentrations were from 23.5 to 50 ng/mL. Ivermectin elimination curve might be subject to enterohepatic recycling. Ivermectin is widely distributed in the body with a volume of distribution about 3.1 and 3.5 L/kg, after ingesting 6 and 12 mg of Ivermectin, respectively. In addition, Ivermectin is approximately 93% bound to plasma proteins, mainly to serum albumin. [8]

Ivermectin is extensively metabolized in vitro by liver microsomal cytochrome P450 3A4 to hydroxylated and demethylated metabolites[15]. Ivermectin and its metabolites appear to be **eliminated mainly in the faeces, with minimal urinary excretion** ($\leq 1\%$ of the administered dose). The mean **half-life of Ivermectin when administered orally is ranging from about 15 to 20 h**

The kinetics of Ivermectin disposition and metabolism in ruminant livestock and horses were reviewed with particular emphasis on the influence of route of administration and it was found out that injection of the subcutaneous formulation of Ivermectin prolongs plasma residence time and persistence of drug residues particularly in liver and fat. Increasing the organic solvent content of subcutaneous formulations slows the release of drug from the injection site and thereby prolongs its presence in the bloodstream. [9]

A specific reversed-phase HPLC-assay with sensitive fluorometric detection has been developed to measure the potent new antiparasitic agent Ivermectin (CAS 70288-86-7) in human plasma (and urine). The lower limit of the method was 1 ng/ml and the intra-/interassay variability averaged 4.5/6.9%, respectively. The assay was applied for measuring plasma (urine) concentrations of Ivermectin upto 56 (72 h) following a single oral dose of 6 and 12 mg. No unchanged or conjugated Ivermectin could be detected in urine. Plasma concentrations increased linearly with dose but elimination half-life (12.6/13.4 h) was independent of the administered dose. Thus, the method is applicable for monitoring plasma levels during clinical and pharmacokinetic trials with Ivermectin to evaluate its most efficacious dosage regimen. [10]

Although the efficacy of Ivermectin has been established in humans against several parasite diseases, the pharmacokinetic properties of this compound are less well known in humans compared to animals. Potential drug-drug interactions and drug-food interactions exist for Ivermectin, which should be considered during therapeutic use of this drug. [11]

Ivermectin has shown effective pharmacological activity towards various infective agents, including viruses. The paper by Emanuele Rizzo proposes an alternative mechanism of action for this drug. **This will make it capable of having an antiviral action, including that against the novel coronavirus.** [12]



D. Bioavailability (BA) and Bioequivalence (BE) Intelligence of Ivermectin [13] [14]

Bioavailability is a measurement of the rate and extent to which a therapeutically active chemical is absorbed from a drug product into the systemic circulation and becomes available at the site of action. For most drugs that are taken orally, the active ingredients are released in the gastrointestinal (GI) tract and arrive at their site of action via the systemic circulation. The relative bioavailability estimate is useful in comparing the extent to which different drug formulations of the same active ingredient are absorbed. If there is a relationship between active moiety plasma concentration and clinical efficacy, knowledge of the bioavailability and disposition kinetics of the active compound would be particularly useful in the development of dosage forms and the comparison of routes of administration.

A guideline for Bioequivalence studies has been included below [15].

Dose: For Ivermectin marketed as 3 mg tablets, the use of a single tablet is recommended to reduce the variability that can be caused by different gastric emptying times of the different tablets, unless a higher therapeutic dose is necessary for bio-analytical reasons (i.e. insufficient lower limit of quantitation to detect levels of 5% of C_{max}). However, if additional strengths are developed in the future in order to simplify the administration by reducing the pill burden, the new higher strengths should be tested unless it is shown that **Ivermectin is a highly soluble drug**.

Fasting/fed: The bioequivalence study should be conducted in the fasting state as Ivermectin should be administered in fasting state.

Subjects: Healthy adult subjects should be used. It is not necessary to include patients in the bioequivalence study.

Analytical considerations: The measurement of Ivermectin B1a in plasma is feasible (LLOQ = 0.2 ng/ml) and the use of the parent drug is considered to be more discriminative to differences in the biopharmaceutical performance of the drug products. Therefore, bioequivalence should be based on the determination of Ivermectin B1a.

Sample size: There is limited data on intra-subject variability of Ivermectin AUC_{0-72h} and C_{max} in humans in the fasting state. These limited data suggest that variability is >30% (approx. 30–40%).

Washout: Taking into account the elimination half-life of Ivermectin in the fasting state of about 53 hours, a washout period of approximately 4 weeks is considered sufficient to prevent carry over. However, this value should be employed cautiously since the existence of enterohepatic recycling may modify this value.

Blood sampling: Blood sampling should be more intensive between 2 and 6 hours after administration to properly characterize the C_{max} of Ivermectin. Considering the elimination half-life, it is sufficient to take blood samples up to 72 hours after administration for the characterization of Ivermectin pharmacokinetics.



Parent or metabolite data for assessment of bioequivalence: The parent drug is considered to best reflect the biopharmaceutical quality of the product. Therefore, bioequivalence should be based on the determination of Ivermectin B1a.

Statistical considerations: The data for Ivermectin should meet the following bioequivalence standards in a single dose, crossover design study:

- The 90% confidence interval of the relative mean AUC_{0-72h} of the test to reference product should be within 80–125%
- The 90% confidence interval of the relative mean C_{max} of the test to reference product should be within 80–125%.

E. Adverse drug event [16]

Ivermectin is a fairly safe drug and acts as an anti-infective agent with activity against several parasitic nematodes and scabies and is the treatment of choice for onchocerciasis (river blindness). It is typically given as one or two oral doses. Ivermectin therapy has been associated with minor, self-limiting serum aminotransferase elevations and very rare instances of clinically apparent liver injury.



Acute Toxicity



Irritant



Health Hazard



Environmental
Hazard

Toxicity: LD₅₀ = 29.5 mg/kg (Mouse, oral). LD₅₀ = 10 mg/kg (Rat, oral).

Adverse effects include muscle or joint pain, dizziness, fever, headache, skin rash, fast heartbeat.

Clinical studies have been carried out to examine the adverse effects of Ivermectin (for diseases other than COVID-19), as seen in the following sections (i) and (ii).

(i) Strongyloidiasis

In four clinical studies involving a total of **109 patients** given either one or two doses of 170 to 200 mcg/kg of STROMEKTOL, the following adverse reactions were reported:

- Body as a Whole:** Fatigue (0.9%), abdominal pain (0.9%)
- Gastrointestinal:** Anorexia (0.9%), constipation (0.9%), diarrhea (1.8%), nausea (1.8%), vomiting (0.9%)



c. Nervous System/Psychiatric: Dizziness (2.8%), somnolence (0.9%), vertigo (0.9%), tremor (0.9%)

d. Skin: Pruritus (2.8%), rash (0.9%), and urticaria (0.9%).

(ii) Onchocerciasis

In clinical trials involving **963 adult patients** treated with 100 to 200 mcg/kg STROMECTOL, worsening of the following Mazzotti reactions during the first 4 days' post-treatment were reported:

- a. Arthralgia/synovitis (9.3%)
- b. Axillary lymph node enlargement and tenderness (11.0% and 4.4%, respectively)
- c. Cervical lymph node enlargement and tenderness (5.3% and 1.2%, respectively)
- d. Inguinal lymph node enlargement and tenderness (12.6% and 13.9%, respectively)
- e. Other lymph node enlargement and tenderness (3.0% and 1.9%, respectively),
- f. Pruritus (27.5%)
- g. Skin involvement including edema, popular and pustular or frank urticarial rash (22.7%)
- h. Fever (22.6%)

Post-Marketing Experience for All Indications

The following adverse reactions have been reported since the drug was registered overseas: hypotension (mainly orthostatic hypotension), worsening of bronchial asthma, toxic epidermal necrolysis, Stevens-Johnson syndrome, seizures, elevation of liver enzymes, and elevation of bilirubin.

Achi community of south-east Nigeria was given mass Ivermectin therapy for onchocerciasis. **7556 subjects were dosed. 992 patients complained** of adverse effects, mostly within one week of dosing. In 962 subjects (97%), adverse events were mild and did not prevent work. Common effects included: Oedema (47.4%), headache (46.4%), and worsening of rash (24.4%)



Clinical Trials and Scientific Publications

A. Exclusion criteria for research

1. Known history of Ivermectin allergy
2. Hypersensitivity to any component of Stromectol
3. COVID-19 Pneumonia
 - a. Diagnosed by the attending physician
 - b. Identified in a chest X-ray
4. Fever or cough present for more than 48 hours
5. Positive IgG against SARS-CoV-2 by rapid test
6. Age under 18 or over 60 years
7. The following co-morbidities (or any other disease that might interfere with the study in the eyes of the investigator): Immunosuppression, Chronic Obstructive Pulmonary Disease, Diabetes, Hypertension, Obesity, Acute or chronic renal failure, History of coronary disease, History of cerebrovascular disease, Current neoplasm
8. Recent travel history to countries that are endemic for Loa loa (Angola, Cameroon, Central African Republic, Chad, Democratic Republic of Congo, Ethiopia, Equatorial, Guinea, Gabon, Republic of Congo, Nigeria and Sudan)
9. Current use of CYP 3A4 or P-gp inhibitor drugs such as quinidine, amiodarone, diltiazem, spironolactone, verapamil, clarithromycin, erythromycin, itraconazole, ketoconazole, cyclosporine, tacrolimus, indinavir, ritonavir or cobicistat. Use of critical CYP3A4 substrate drugs such as warfarin.

B. Research 1: Pivoting point that brought spotlight on Ivermectin - Monash research



Background:

The research on Ivermectin for COVID-19 came into consideration due to a collaborative study by Monash University's Biomedicine Discovery Institute (BDI) and the Peter Doherty Institute of Infection and Immunity (Doherty Institute), both in Australia. The study was led by Dr. Kylie Wagstaff, along with Professor David Jans, both from BDI.

Dr. Wagstaff had made a previous breakthrough finding on Ivermectin in 2012, when she identified the drug and

its antiviral activity along with Professor David Jans, who has been researching Ivermectin's



antiviral properties for more than 10 years with different viruses. Dr. Wagstaff and Professor Jans began their work on SARS-CoV-2 as soon as the pandemic was reported to have started [17].

Research details [18]:

- i. Methodology 1: The antiviral activity of Ivermectin towards SARS-CoV-2 was studied by infecting Vero/hSLAM cells with SARS-CoV-2 isolate Australia/VIC01/2020 at an MOI of 0.1 for 2 h, followed by the addition of 5 μ M Ivermectin. Supernatant and cell pellets were harvested at days 0–3 and analysed by RT-PCR for the replication of SARS-CoV-2 RNA.
- ii. Results 1: **At 24 h, there was a 93% reduction in viral RNA present** in the supernatant (indicative of released virions) of samples treated with Ivermectin compared to the vehicle DMSO. Similarly, a 99.8% reduction in cell-associated viral RNA (indicative of unreleased and unpackaged virions) was observed with Ivermectin treatment. **By 48 h this effect increased to an ~5000-fold reduction of viral RNA** in Ivermectin-treated compared to control samples, indicating that Ivermectin treatment resulted in the effective loss of essentially all viral material by 48 h. Consistent with this idea, no further reduction in viral RNA was observed at 72 h. Further, no toxicity of Ivermectin was observed at any of the time points tested, in either the sample wells or in parallel tested drug alone samples.
- iii. Methodology 2: To further determine the effectiveness of ivermectin, cells infected with SARS-CoV-2 were treated with serial dilutions of Ivermectin 2 h post infection and supernatant and cell pellets collected for real-time RT-PCR at 48 h.
- iv. Results 2: Similar to the aforementioned results, a **>5000 reduction in viral RNA was observed in both supernatant and cell pellets from samples treated with 5 μ M Ivermectin at 48 h**, equating to a 99.98% reduction in viral RNA in these samples. Again, **no toxicity was observed** with Ivermectin at any of the concentrations tested. The IC₅₀ of Ivermectin treatment was determined to be ~2 μ M under these conditions.

Conclusion:

The in vitro studies demonstrated that Ivermectin can stop SARS-CoV-2 growth in cell cultures by eradicating all genetic information within two days. An Ivermectin dose of 5 μ M had an inhibitory action on the novel coronavirus, **reducing the load of viral RNA by 5,000 times in 48 hours**. These findings were published in Antiviral Research. As a result, researchers all around the world started studying the effect of Ivermectin on SARS-CoV-2. In vivo studies (clinical trials) have also started around the world.

Key Findings:

- Ivermectin is an inhibitor of the COVID-19 causative virus (SARS-CoV-2) in vitro.
- A single treatment gives **~5000-fold reduction in virus at 48 h** in cell culture.
- Ivermectin is FDA-approved for parasitic infections, and therefore has a potential for repurposing.
- Ivermectin is **widely available**, due to its inclusion on the WHO model list of essential medicines.



Research 2: ICON (Ivermectin in COVID Nineteen) Study [19]

Background:

As of May 24th, 2020, the CDC recorded nearly 100,000 people having died of Covid-19 with at least 1,639,099 confirmed infections having been reported in the US and its territories. Covid-19 presents an unprecedented challenge to identify effective therapy for prevention and treatment. Currently, there is no evidence from randomized controlled trials of any potential therapy improving survival outcomes in patients with confirmed disease.

Ivermectin has previously been studied as a therapeutic option for viral infections with in vitro data showing some activity against a broad range of viruses, including HIV, Dengue, Influenza and Zika virus.^{2,3} In a recent study, Wagstaff et al, demonstrated that Ivermectin was a potent in-vitro inhibitor of SARS-CoV-2, showing a **99.8% reduction in viral RNA after 48 hours**. However, in-vivo efficacy of Ivermectin in SARS-CoV-2 infection in humans has not previously been reported.

Research details:

Methodology: Patients in the Ivermectin group received at least one oral dose of Ivermectin at 200 micrograms/kilogram in addition to usual clinical care. The decision to prescribe Ivermectin, hydroxychloroquine, azithromycin or other medications was at the discretion of the treating physicians, however hospital guidelines were established for the use of these agents as well as for cardiac and QT monitoring for patients receiving hydroxychloroquine. Oxygen and ventilatory support were applied per the customary care.

Results: The primary outcome was all-cause in-hospital mortality. Patients were considered a “survivor” if they left the hospital alive, or if their status in the hospital changed from active care to awaiting transfer to a skilled facility. The latter outcome was necessitated by the requirement that two consecutive negative nasopharyngeal swab specimens for SARS-CoV-2, collected equal to or greater than 24 hours apart, were necessary for a patient to be accepted to a skilled nursing facility. Secondary outcomes included subgroup mortality of patients with severe pulmonary involvement, extubation rates for patients requiring mechanical ventilation, and length of hospital stay.

Conclusion:

Overall mortality was significantly lower in the Ivermectin group than in the usual care group (15.0% vs 25.2%, for Ivermectin and usual care respectively, $p=.03$). Mortality was also lower for Ivermectin treated patients in the subgroup of patients **with severe disease (38.8% vs. 80.7%, $p=.001$). Differences in extubation rates between groups were not significant and there was also no difference in length of hospital stay.**



Key Findings:

- Ivermectin administration was significantly associated with lower mortality among patients with COVID-19, particularly in patients with more severe disease.
- The Cox regression showed Ivermectin was associated with a significantly lower hazard ratio for mortality of 0.37 (CI 0.19 - 0.70, $p=.003$).

C. Trials of Ivermectin across the world

Several studies have been planned by universities, institutes and hospitals across the globe. The **USA themselves have planned 18 randomized controlled studies** and trials for Ivermectin on covid. Few other trials for Ivermectin include:



University of Tanta, and Mansoura University, Egypt: The study's participants will receive a combination of Nitazoxanide, Ribavirin and Ivermectin for a duration of seven days. Launched on April 15 2020, the first Tanta University **Phase II/III** randomized, parallel assigned, five arm study, involves up to 100 patients with COVID-19. In both studies, the Principal Investigator, Sherief Abd-Elsalam, associate professor Faculty of Medicine, looks to a primary endpoint involving the total number of patients with virological cure over a duration of six-month period. [\[20\]](#)



University of Baghdad, Iraq: This influential Middle East institution of higher learning is comparing in this Phase I study, the efficacy and safety of Use of Ivermectin in COVID-19 patients with pneumonia. Ivermectin 0.2 mg/kg (12 mg adult dose) single dose is repeated after 1 week combined with hydroxychloroquine 400 mg daily compared to Hydroxychloroquine, plus placebo single one dose repeated after 1 week. Put another way, **they want to see if adding Ivermectin to Hydroxychloroquine makes a difference** to those infected with COVID-19. The study started April 18, 2020 and runs through until August 2020. 50 participants have been enrolled for the research. [\[21\]](#)



General Directorate of Medical City, Iraq: The Phase I trial that began on April 13, 2020 and **completed on 5 June 2020**. It was aimed at finding the Efficacy of Ivermectin as Add on Therapy in COVID19 Patients. Primary endpoint was Number of cured patients in 4 weeks while secondary endpoint was Mean time to cure the COVID-19 patients. [22]



University of Kentucky (UK), USA: The trial will investigate the effectiveness of azithromycin, Ivermectin and camostat mesylate—drugs that could inhibit replication of SARS-CoV-2, the virus that causes the disease. The three will be tested either as stand-alone therapies or in combination with the antimalarial drug hydroxychloroquine. **The trial has a “pick-the-winner” design**, which will allow UK researchers to rapidly understand what potential therapies appear to be effective, guiding patients to treatments that work and researchers to promising drugs that warrant further investigation. [23]



Johns Hopkins University, USA: Planned to commence June 2020 for a year, the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins will probe into **whether bicalutamide or Ivermectin can have an impact on hospitalized patients** infected with SARS-CoV-2. [24]



Clinica Universidad de Navarra, Spain: The study has been titled as Sars-CoV-2/COVID-19 Ivermectin Navarra-ISGlobal Trial (SAINT). SAINT is a double-blind, randomized controlled trial with two parallel groups that evaluates the **efficacy of Ivermectin in reducing nasal viral carriage at seven days** after treatment in SARS-CoV-2 infected patients who are at low risk of progression to severe disease. The trial is currently planned at a single center in Navarra. Primary endpoint is to determine the proportion of patients with a positive SARS-CoV-2 PCR from a nasopharyngeal swab at day 7 post-treatment. [25]



Combined Military Hospital Lahore, Pakistan: This randomized, controlled trial has been designed to investigate the efficacy of Ivermectin in COVID-19 patients. Patients will be assigned to two groups, including 1) that will be given Ivermectin with standard chloroquine regimen, and 2) the other group will be given chloroquine only. The outcomes will be recorded by documenting PCR reports at 48, 96 and 144 hours. **The study was launched April 15, 2020 and runs till July 2020.** Recruiting 100 patients, the study precludes those with severe conditions or comorbidities such as malignant disease, diabetes, etc. [26]



Laboratorio Elea Phoenix S.A., Argentina: Argentina's Laboratorio Elea Phoenix S.A. (Elea Laboratories) has initiated a proof-of-concept clinical trial with 45 patients to investigate the efficacy of Ivermectin as a treatment for patients infected with SARS-CoV-2. The South American pharmaceutical company based its decision on the important Monash University lab study plus the fact that Ivermectin has been widely in use for decades. [27]

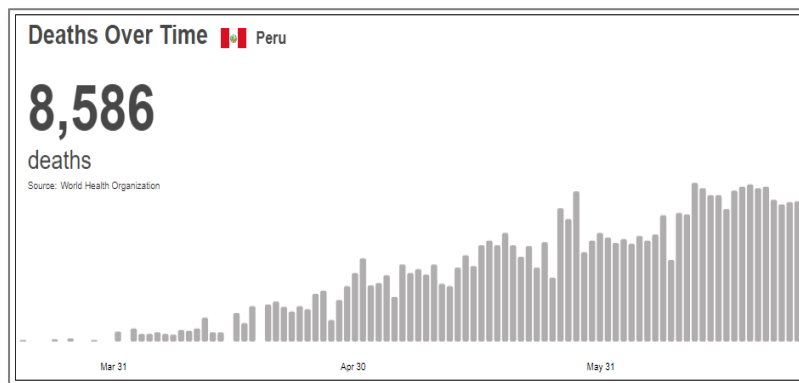


Jose Manuel Arreola Guerra (Researcher): The study seeks to investigate the safety and efficacy of a treatment involving hydroxychloroquine and Ivermectin for serious COVID-19 infections in non-critical hospitalized patients. Prior to any patient randomization the investigational team will assess cardiovascular complications determined by the corrected QT interval, related to hydroxychloroquine intake. For example, **if a patient is at high risk, they will be placed in an Ivermectin group** only or to placebo in an independent randomization [28]

Use of Ivermectin across the world

Apart from the number of study, research and clinical trials going around, some nations have permitted use of Ivermectin. We have discussed a few of them in brief.

A. Peru



Peru has accepted Ivermectin as a COVID-19 treatment, however the government's decision was not based on formal, randomized controlled trials. Instead, a network of many doctors in and around Peru drove a kind of community movement to use the medicine to treat COVID-

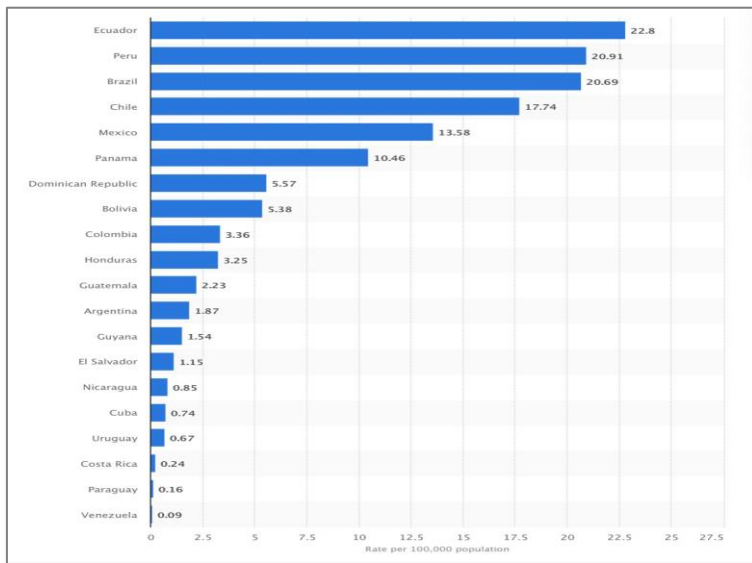
19. Doctors started using Ivermectin and reporting positive results to colleagues. The government came to the conclusion that a sufficient number of experts in the country had formed a consensus that could not be ignored [29]. Thus, Ivermectin is being used on a wide scale in Peru, in combination with other drugs like hydroxychloroquine, azithromycin and chloroquine phosphate. Dosage forms for the treatment of mild, moderate and severe forms of COVID-19, using the above combinations, have been established [30].

B. Bangladesh:

Following the Monash-Doherty research, physicians at a Dhaka hospital have observed cumulative efficacy of a combination therapy of Ivermectin and doxycycline in Covid-19 patients. The medication was tested in 60 patients who were staff members of Bangladesh Medical College and Hospital. After 72 hours of drug administration, the majority of the patients' conditions started improving. The average recovery time was noted to be 11 days. **Out of 60 COVID-19 patients, all recovered as the combination of the two drugs were applied.** This paved way for clinical trials. The doctors have stated that Ivermectin should not be administered to pregnant or breastfeeding women, children under five or weighing below 15 kg, and patients with liver diseases. After successful clinical trials, they have concluded that Ivermectin gives promising results in mild cases, however, it remains ineffective in patients with severe conditions [31].



C. South Americas:



South American Nations like Peru, Bolivia, have been using Ivermectin to fight against COVID-19. It has been reported that **many provinces have already approved Ivermectin as a treatment for SARS-CoV-2**, the virus behind COVID-19. While Argentina is carrying out clinical trials, many other countries have started using the drug without concrete scientific proof of its effects in a vast population. For example, Trinidad, a city in Bolivia, initiated a campaign to combat

COVID-19 by distributing free doses of the anti-parasite drug in an effort to take on the pathogen in the eastern region of the country where more have contracted the virus [32]. Thus, there is a growing interest and even authorization of Ivermectin in some of the more economically challenged South American nations [33].



On the left is image of Manuel Negrete, **former Mexican footballer** as he holds the anti-parasite drug Ivermectin after buying it with a medical prescription at a local pharmacy in Santa Cruz, Bolivia May 19, 2020. REUTERS/Rodrigo Urzagasti

WHO Bulletin:



The World Health Organization bulletin on Ivermectin covers its veterinary drug history followed by its potential for human use. It has valuable public health applications for controlling strongyloidiasis, scabies and filariasis. Ivermectin also acts against other intestinal nematodes, but it is not the most effective drug available. In control programmes for filariasis, Ivermectin is the drug of choice in areas with onchocerciasis, but can be replaced by diethylcarbamazine for control of other filarial diseases.

It is time to capitalize on the full public health potential of Ivermectin. Carefully designed studies to evaluate the efficacy of community-wide Ivermectin based control programmes for strongyloidiasis and scabies in developing countries are indicated, as are similar studies in marginalized communities in developed countries with high prevalence of these two diseases, including indigenous communities in Australia [34].

A. WHO: Mass treatment with Ivermectin - an underutilized public health strategy [35]

WHO, in their bulletin posted an issue stating the need to realize the full public health potential of Ivermectin. Ivermectin has historically proved to be of valuable public health applications such as controlling strongyloidiasis and scabies. It has helped in breaking the infection cycle through its therapeutic effect and filariasis, through its effect on transmission.

A study has been mentioned that investigates changes in parasitological parameters and the occurrence of side-effects after treatment with Ivermectin. The treatment was for a Brazilian community, heavily parasitized with intestinal helminths and ectoparasites. Community members, ineligible for Ivermectin, were treated with mebendazole, albendazole or deltamethrin to achieve a high level of coverage. The findings of Ivermectin were highly effective against *Strongyloides stercoralis*, with a 94% reduction in prevalence that was sustained for nine months. This provided field evidence for a paper that predicted that strongyloidiasis in heavily endemic communities could be successfully controlled with a highly effective drug, owing to its low transmission potential. If similar success is achieved with COVID, it can be a huge relief globally. This and the aim of realizing the potential of Ivermectin is possible only through detailed and fast tracked trial of the drug.



B. WHO mass drug administration of Ivermectin

As discussed above, Onchocerciasis (also known as river blindness) can lead to blindness and severe, debilitating skin irritation. Mass drug administration of Ivermectin 1 or 2 times annually (for 10-20 years) to control or eliminate onchocerciasis. High-quality evaluations have demonstrated that Ivermectin is effective in suppressing the worms that cause onchocerciasis. [36]

Ivermectin is widely used in mass drug administrations for controlling neglected parasitic diseases, and can be lethal to malaria vectors that bite treated humans. The hypothesis of frequently repeated mass administrations of Ivermectin to village residents was tested. It reduces clinical malaria episodes in children and would be well tolerated with minimal harms. It could be a powerful and synergistic new tool to reduce malaria transmission in regions with epidemic or seasonal malaria transmission, and the prevalence and intensity of neglected tropical diseases. [37]

Scabies was added to the World Health Organization list of neglected tropical diseases. Scabies is a skin disease caused by a mite that burrows under the skin and is transmitted through prolonged skin-to-skin contact. Mass drug administration (MDA) campaign was adopted to treat scabies with oral Ivermectin. In small community-based trials, mass drug administration of Ivermectin has been shown to substantially decrease the prevalence of both scabies and secondary impetigo. In 2018, **Ivermectin was proposed for inclusion on the WHO Model List of Essential Medicines (EML) and Model List of Essential Medicines for Children (EMLc) for the indication of Scabies.**[38]



Ivermectin in India against COVID-19

The use and study of Ivermectin is not just limited to outside India. Even in India, several doctors are of the view that Ivermectin can be a top candidate for curing COVID. One example of such covered use of Ivermectin is from the city that has the leading number of corona cases.

A. Use in Mumbai Hospital

In hospitals of Mumbai, Ivermectin is being given to the patients in combination with doxycycline. **It is administered to those having heart rhythm problems and who cannot be given the usual combination of antimalarial drug HCQS and antibiotic.** The state task force advised its use. The Maharashtra task force members spoke to the doctors from Bangladesh and felt it could be used in India as well. Dr. Gautam Bhansali from Bombay Hospital said **20-30 patients in the hospital have been given the combination.** Infectious diseases specialist Dr. Om Srivastava said the combination has to be studied before it can be widely advised.[39]

B. Trials in the country [40]

Clinical trials registry- India (CTRI) at ICMR- National Institute of Medical Statistics is an online public record system for registration of clinical trials being conducted in India. The mission of CTRI is to encourage all clinical trials conducted in India to be prospectively registered, i.e. before the enrolment of the first participant.

Clinical trials related to Ivermectin and COVID-19. **All of the trials for Ivermectin as a treatment of COVID-19 in India are either in the recruitment phase or not recruiting phase. There is a need to fast track the trials for a drug with such high candidature.**



Sr. No	CTRI No.	Public Title	Type of Trial	Recruitment Status	Health Condition	Intervention Name	Location
1	CTRI/2020/04/024858	"To study the effectiveness of Ivermectin with standard of care treatment versus standard of care treatment for COVID 19 cases. A Pilot Study	Interventional	Total: Not Applicable Indian: Not Yet Recruiting	Other specified viral diseases	Ivermectin	Max Super Specialty hospital, Saket (A unit of Devki Devi Foundation),DELHI
2	CTRI/2020/04/024948	A clinical Trial to Study the Effects of Hydroxychloroquine, Ciclesonide and Ivermectin in treatment of moderate COVID-19 illness	Interventional	Total: Not Applicable Indian: Not Yet Recruiting	Coronaviruses as the cause of diseases classified elsewhere Other specified viral diseases	Hydroxychloroquine Ciclesonide Ivermectin	Department of Medicine,DELHI



Sr. No	CTRI No.	Public Title	Type of Trial	Recruitment Status	Health Condition	Intervention Name	Location
3	CTRI/2020/05/025068	Can a medicine help in curing viral infection	Interventional	Total: Not Applicable Indian: Not Yet Recruiting	Other specified viral diseases	Ivermectin	Christian Medical College Vellore, TAMIL NADU
4	CTRI/2020/05/025224	Study to efficacy of Ivermectin in patients of COVID-19	Interventional	Total: Not Applicable Indian: Not Yet Recruiting	Coronaviruses as the cause of diseases classified elsewhere	Ivermectin	R D Gardi Medical College, Ujjain, MADHYA PRADESH
5	CTRI/2020/05/025333	Study to assess efficacy of Ivermectin as prophylaxis of COVID -19	Interventional	Total: Not Applicable Indian: Not Yet Recruiting	Healthy health care workers or Healthy contact of COVID 19	Ivermectin	R D Gardi Medical College, Ujjain, MADHYA PRADESH
6	CTRI/2020/06/025960	To study effect of Ivermectin drug in patients infected with SARS-CoV-2 virus.	Interventional	Total: Not Applicable Indian: Not Yet Recruiting	Coronaviruses as the cause of diseases classified elsewhere	Tablet Ivermectin	Symbiosis University Hospital and Research Centre, MAHARASHTRA



Indian production of Ivermectin [\[41\]](#) [\[42\]](#) [\[43\]](#) [\[44\]](#)

Indian pharmaceutical industry has the **largest number of US Food and Drug Administration (USFDA) approved manufacturing facilities outside the US**, and over 1,300 manufacturing plants compliant with the World Health Organization (WHO) Good Manufacturing Practices. Following is the record of brand names under which Ivermectin is sold in India

Brand Name	Composition	Company	Quantity	MRP Rs.
AGIMECT tab	Ivermectin 12mg	AEGIS PHARMACEUTICALS	4	175
ASCAPIL tab	Ivermectin 6mg	NICHOLAS PRIMAL INDIA	1	16.27
ASCAPIL tab	Ivermectin 6mg	AHPL	4	65.09
AVERM PLUS	Ivermectin 12mg	BIOTAVIA LABS		105
BANDY PLUS tab	Ivermectin 6mg, albendazole 400mg	MANKIND PHARMA	1	23.90
BANDY PLUS tab	Ivermectin 12mg, albendazole 400mg	MANKIND PHARMA	1	28.80
BENDEX PLUS tab	Ivermectin 6mg, albendazole 400mg	CIPLA	1	26.40
BIOVER tab	Ivermectin 6mg	BIOGENETIC PHARMACEUTICALS	10	150
ECTIN tab	Ivermectin 6mg	ELFIN PHARMA	40	380
ECTOVER tab	Ivermectin 12mg	WORTH MRDICINES	10	199



Brand Name	Composition	Company	Quantity	MRP Rs.
ELECT DT tab	Ivermectin 6mg	CAPTAB BIOTEC	60	960
ELECT DT tab	Ivermectin 12mg	CAPTAB BIOTEC	60	1500
EVERGRIN-A tab	Ivermectin 6mg, albendazole 400mg	GENETIC PHARMA	1	18.72
EVERGRIN-A susp	Ivermectin 1.5mg, albendazole 200mg/5ml	GENETIC PHARMA	1	28.00
EVERSON tab	Ivermectin 6mg	PARKINSON PHARMA	10	N.A.
EVERSON-A tab	Ivermectin 6mg, albendazole 400mg	PARKINSON PHARMA	10	N.A.
EVERTIN-6 tab	Ivermectin 6mg	ZEE LABORATORIES	4	59
EVRIINA tab	Ivermectin 3mg	PRIDE HEALTHCARE		500
EVRIINA tab	Ivermectin 6mg	PRIDE HEALTHCARE		750
HESTIN tab	Ivermectin 3mg	ARTICON LABS		37.79
HESTIN tab	Ivermectin 6mg	ARTICON LABS		63
I-STAR tab	Ivermectin 6mg	ORGANIC LABS		48
IMEC-H tab	Ivermectin 12mg	GARY PHARMACEUTICALS		25
IMEC-M tab	Ivermectin 6mg	GARY PHARMACEUTICALS		13



Brand Name	Composition	Company	Quantity	MRP Rs.
IMECTIN tab	Ivermectin 3mg	PULSE PHARMACEUTICALS	2	15
IMECTIN tab	Ivermectin 6mg	PULSE PHARMACEUTICALS	2	20
IMECTIN tab	Ivermectin 12mg	PULSE PHARMACEUTICALS	2	30
INOVER tab	Ivermectin 3mg	H. L. HEALTHCARE		8
INOVER tab	Ivermectin 6mg	H. L. HEALTHCARE		12
ISCO tab	Ivermectin 3mg	BENNET PHARMACEUTICALS		32
IVAZED tab	Ivermectin 6mg	ZEDCHEM PHARMA		16
IVECOP-DT tab	Ivermectin 3mg	SHALAKS PHARMACEUTICALS	2	11.60
IVECOP tab	Ivermectin 6mg	SHALAKS PHARMACEUTICALS	1	10.50
IVECOP tab	Ivermectin 12mg	SHALAKS PHARMACEUTICALS	1	15.60
IVEL tab	Ivermectin 6mg	DERMAVIN PHARMACEUTICALS		9
IVEL 12 tab	Ivermectin 12mg	DERMAVIN PHARMACEUTICALS		16



Brand Name	Composition	Company	Quantity	MRP Rs.
IVER-A tab	Ivermectin 6mg, albendazole 400mg	SHRI PHARMA	1	N.A.
IVERCID tab	Ivermectin 3mg	EAST WEST PHARMA	2	19.8
IVERCID tab	Ivermectin 6mg	EAST WEST PHARMA	2	30
IVERCID tab	Ivermectin 12mg	EAST WEST PHARMA	2	48
IVERDIS tab	Ivermectin 6mg	MEDIS LAB (PRAGATI BIOCARE)	4	64
IVERDIS tab	Ivermectin 12mg	MEDIS LAB (PRAGATI BIOCARE)	4	95
IVERFAST-12 tab	Ivermectin 12mg	SUBODH IMPEX		280
IVERFAST tab	Ivermectin 12mg	HERAMB HEALTHCARE		18
IVERIN tab	Ivermectin 3mg	SATVEN AND MER	2	13
IVERIN D S tab	Ivermectin 6mg	SATVEN AND MER	2	19
IVERIN tab	Ivermectin 12mg	SATVEN AND MER	10	220
IVERIV tab	Ivermectin 12mg	EAST AFRICAN (INDIA) REMEDIES	100	1860
IVERMECTOL tab	Ivermectin 3mg	OCHOA	1	23.50



Brand Name	Composition	Company	Quantity	MRP Rs.
IVERMECTOL tab	Ivermectin 6mg	OCHOA	2	42
IVERMECTOL tab	Ivermectin 12mg	OCHOA	2	77.50
IVERMECTOL tab	Ivermectin 3mg	SUN PHARMACEUTICAL		23.50
IVERMECTOL tab	Ivermectin 6mg	SUN PHARMACEUTICAL		42
IVERMECTOL tab	Ivermectin 12mg	SUN PHARMACEUTICAL		85
IVERPIL tab	Ivermectin 6mg	PSYCHOTROPICS INDIA		22
IVERPIL tab	Ivermectin 12mg	PSYCHOTROPICS INDIA		15.98
IVERSCAB tab	Ivermectin 6mg	NuLIFE PHARMACEUTICALS		39
IVERSCAB tab	Ivermectin 12mg	NuLIFE PHARMACEUTICALS		53
IVERT tab	Ivermectin 6mg	TRIPADA BIOTEC		60
IVERT tab	Ivermectin 12mg	TRIPADA BIOTEC		90
IVER SOL 3 tab	Ivermectin 3mg	PSYCO REMEDIES	20	140
IVER SOL 6 tab	Ivermectin 6mg	PSYCO REMEDIES	20	240



Brand Name	Composition	Company	Quantity	MRP Rs.
IVER SOL 12 tab	Ivermectin 12mg	PSYCO REMEDIES	20	440
IV PAC tab	Ivermectin 6mg	PACIFIC INDIA		40
MECTIN tab	Ivermectin 3mg	MERIDIAN	1	8
MECTIN tab	Ivermectin 6mg	MERIDIAN	1	12.80
MECTIN tab	Ivermectin 12mg	MERIDIAN	1	15.00
MERIBEN tab	Ivermectin 6mg, albendazole 400mg	MERIDIAN	1	22.50
MERIBEN susp	Ivermectin 3mg, albendazole 200mg/5ml	MERIDIAN	10mL	30.80
SCABERASE IF tab	Ivermectin 12mg	ROWAN BIOCEUTICALS		19.8
SCABERASE IM	Ivermectin 6mg	ROWAN BIOCEUTICALS		47.97
SCAVISTA tab	Ivermectin 3mg	ZUVENTUS	1	11.80
SCAVISTA tab	Ivermectin 6mg	ZUVENTUS	1	17.70
SCAVISTA tab	Ivermectin 12mg	ZUVENTUS	1	29.50
SIVERMIN tab		SAIMARK BIOTECH		
SIVERMIN tab		SAIMARK BIOTECH		



Brand Name	Composition	Company	Quantity	MRP Rs.
SKINTIN tab	Ivermectin 6mg	AMRAY	1	18
SKINTIN tab	Ivermectin 12mg	AMRAY	1	25
TERGUM tab	Ivermectin 6mg	BIOSCIENCES PHARMAKON	1	17
TROMER tab	Ivermectin 6mg	ELFIN PHARMA	40	380
VARZO tab	Ivermectin 6mg	ZODAK	1	12.60
VERMACT tab	Ivermectin 3mg	MANKIND PHARMA		11.26
VERMACT tab	Ivermectin 6mg	MANKIND PHARMA		22.62
VERMACT tab	Ivermectin 12mg	MANKIND PHARMA		37.26
VERMECTIN tab	Ivermectin 6mg	MICRO VISION	1	15.00
VERMECTIN tab	Ivermectin 12mg	MICRO VISION	1	22.52
VERMIN tab	Ivermectin 6mg	HALEDEW	1	16
VERMIN tab	Ivermectin 12mg	HALEDEW	1	20
VERMISCAB tab	Ivermectin 6mg	SIGMAN	1	16
VERMISCAB tab	Ivermectin 12mg	SIGMAN	1	20
VERMIZOLE tab	Ivermectin 6mg,	FITWEL	1	20



	albendazole 400mg	PHARMACEUTICALS		
Brand Name	Composition	Company	Quantity	MRP Rs.
VERSIL-6	Ivermectin 6mg	SANIFY (SILVER BIOTECH)	1	15
WARMY PLUS susp	Ivermectin 1.5mg, albendazole 200mg	ESQUIRE DRUG HOUSE	10mL	38.00
XULTIVER-6 tab	Ivermectin 6mg	SYNTONIC LIFE SCIENCES	1	N.A.
XULTIVER-A tab	Ivermectin 6mg, albendazole 400mg	SYNTONIC LIFE SCIENCES	1	N.A.



Comparison of Ivermectin and drugs available for COVID Treatment

Parameters	Dexa-methasone	Remdesivir	Favipiravir	Hydroxy-chloroquine	Ivermectin
Cost	Rs. 100 to Rs.200 for a day's dose	Rs. 5000 per vial	Rs.103 per tablet	Rs. 60 to Rs.100 per strip	Rs. 9 to Rs.100 per strip
Side Effect	Swelling, rapid weight gain, headache, dizziness, nausea, bloating, muscle weakness	Adverse Liver and Kidney risk, nausea, diarrhea,	Potential for teratogenicity and embryo toxicity in humans	Headache, dizziness, diarrhea, stomach cramps, vomiting	Headache dizziness, muscle pain, nausea
Primary Endpoint	Improved 28-day mortality	Discharged alive from hospital	Viral Clearance time	In-hospital mortality	Mean day of hospital stay
Secondary Endpoint	Reduced need for intubation and reduced hospital length of stay	Reduction in viral load	Chest imaging improvement rate	Occurrence of clinically significant ventricular arrhythmias	Mean time to viral PCR negativization
Patent	Generic	Patented	Patented	Generic	Generic
Stage of use	Moderate to severe	Moderate to severe	Initial to moderate	Moderate to severe	Initial to moderate



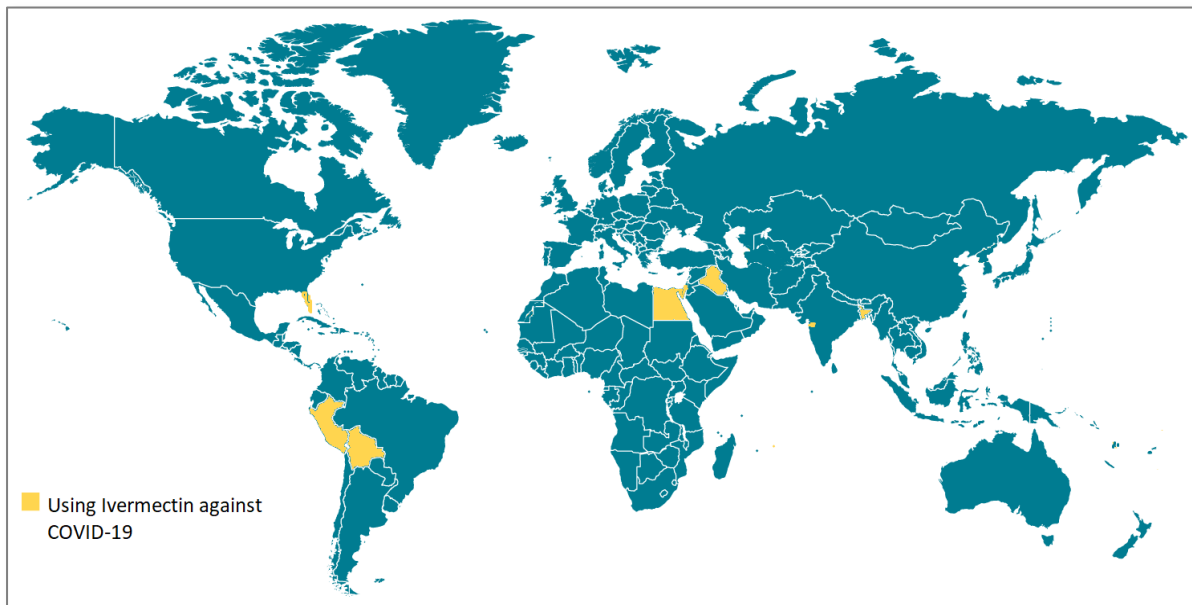
Conclusion

The antiviral effects of Ivermectin on a broad range of RNA and DNA viruses have been studied since 1970. **Clinical trials around the world have shown the possibility that Ivermectin could be a useful antiviral agent in several viruses including those with positive-sense single-stranded RNA, in similar fashion.** Since significant effectiveness of Ivermectin is seen in the early stages of infection in experimental studies, it is proposed that Ivermectin administration may be effective in the early stages or prevention.

Ivermectin, owing to its antiviral activity, **may play a pivotal role in several essential biological processes; therefore it could serve as a potential candidate in the treatment of different types of viruses including COVID-19.**



Future research area



The recent findings regarding Ivermectin warrant rapidly implemented controlled clinical trials to assess its efficacy against SARS-CoV-2. These trials may open a new field of research on the potential use of Ivermectin antiparasitic drugs, including compounds with an improved pharmacokinetic profile, as antivirals.

However, because of the following points, extreme due diligence and regulatory review are needed before testing Ivermectin in severe disease.

(1) Ivermectin, which targets glutamate-gated chloride channels in invertebrates, may cross-target the GABA-gated chloride channels present in the mammalian central nervous system (CNS) and cause neurotoxicity.¹⁹ This is normally prevented by an intact blood–brain barrier (BBB), but in patients with a hyperinflammatory state, endothelial permeability at the BBB may be increased and cause leaking of drugs into the CNS, potentially causing harm.^{20,21}

(2) Boosted antiretrovirals such as lopinavir/ritonavir and darunavir/cobicistat, which have been widely used against SARS-CoV-2 based on limited evidence, and a number of other drugs, are potent inhibitors of cytochrome P450 3A4, the main metabolic pathway for Ivermectin. Concurrent use of these drugs will result in increased systemic exposure to Ivermectin. Furthermore, ritonavir and cobicistat can readily inhibit one of the main efflux pumps in the BBB, P-glycoprotein, further favoring neurotoxicity.^{22,23} However, it is encouraging that a recent analysis of Ivermectin-related neurotoxic adverse events reported to the WHO Program for International Drug Monitoring found only one case of 1,668 reports in which concomitant use of antivirals was associated with neurotoxicity.^[45]

A path to consider is evaluation first of impacts on virologic outcomes in uncomplicated, low-risk patients early in the course of the disease. **This is imperative to stop the spread of viruses further and reduce the number of active cases. If Ivermectin is able to do that, it will be of huge help to the already crumbling health infrastructure globally.** With positive results in trial, few countries approving it as a drug for COVID and the ability of India to produce Ivermectin on a large scale, it becomes very important for India to speed up their clinical trials on Ivermectin.



References

- [1] <https://www.nature.com/articles/s41429-020-0336-z.pdf>
- [2] <https://www.sciencedirect.com/science/article/pii/S0166354220302011>
- [3] A. Crump and S. Omura, "Ivermectin, 'Wonder drug' from Japan: The human use perspective," *Proc. Japan Acad. Ser. B Phys. Biol. Sci.*, vol. 87, no. 2, pp. 13–28, 2011.
- [4] The International Pharmacopoeia, "19th WHO Model List of Essential Medicines," <Http://Www.Who.Int/Medicines/Publications/Essentialmedicines/En>, no. April, pp. 1–43, 2015.
- [5] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3043740/>
- [6] <https://www.tandfonline.com/doi/full/10.1080/13102818.2020.1775118>
- [7] <https://www.medrxiv.org/content/10.1101/2020.04.11.20061804v1.full.pdf>
- [8] <https://www.wjgnet.com/2218-6190/full/v5/i1/57.htm>
- [9] <https://www.sciencedirect.com/science/article/abs/pii/S030440179390143B?via%3Dihub>
- [10] <https://europepmc.org/article/med/8329009#impact>
- [11] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2751445/>
- [12] <https://link.springer.com/article/10.1007/s00210-020-01902-5>
- [13] "Notes on the design of bioequivalence study: Ivermectin," 2019.
- [14] G. Suarez, L. Alvarez, D. Castells, and R. Ungerfeld, "Bioequivalence Assessment of three Ivermectin oral formulations in lambs," vol. 1, no. 1, 2000.
- [15] "Notes on the design of bioequivalence study," *WHO/PQT Med.*, no. April, pp. 3–4, 2008.
- [16] PubChem, "Ivermectin." [Online]. Available: <https://pubchem.ncbi.nlm.nih.gov/compound/Ivermectin#section=Safety-and-Hazards>. [Accessed: 19-Jun-2020].
- [17] H. Balfour, "Ivermectin shows activity against COVID-19 in cell cultures," *Drug Target Review*, 2020.
- [18] L. Caly, J. D. Druce, M. G. Catton, D. A. Jans, and K. M. Wagstaff, "The FDA-approved drug Ivermectin inhibits the replication of SARS-CoV-2 in vitro," *Antiviral Res.*, vol. 178, p. 104787, 2020.
- [19] https://www.researchgate.net/publication/342056504_ICON_Ivermectin_in_COvid_Nineteen_study_Use_of_Ivermectin_is_Associated_with_Lower_Mortality_in_Hospitalized_Patients_with_COVID19
- [20] <https://www.trialsitenews.com/tanta-university-pi-sponsors-ivermectin-studies-targeting-covid-19-in-up-to-160-patients-while-safety-is-a-concern-for-regulators/>
- [21] <https://www.trialsitenews.com/university-of-baghdad-launches-ivermectin-clinical-trial-for-covid-19-patients/>
- [22] <https://www.sciencemag.org/news/2020/06/mysterious-company-s-coronavirus-papers-top-medical-journals-may-be-unraveling>



- [23] <http://uknow.uky.edu/research/uk-launches-clinical-trial-evaluate-novel-treatments-covid-19>
- [24] <https://clinicaltrials.gov/ct2/show/NCT04374279>
- [25] <https://clinicaltrials.gov/ct2/show/NCT04390022>
- [26] <https://www.trialsitenews.com/combined-military-hospital-pakistan-launches-ivermectin-clinical-trial-investigating-efficacy-in-covid-19-patients/>
- [27] <https://www.trialsitenews.com/argentinian-pharma-elea-laboratories-launches-poc-clinical-trial-investigating-ivermectin-in-hospitalized-covid-19-patients/>
- [28] <https://clinicaltrials.gov/ct2/show/NCT04381858>
- [29] “How a Grass Roots Health Movement Led to Acceptance of Ivermectin as a COVID-19 Therapy in Peru,” Trial Site News, 2020. [Online]. Available: <https://www.trialsitenews.com/how-a-grass-roots-health-movement-led-to-acceptance-of-ivermectin-as-a-covid-19-therapy-in-peru/>. [Accessed: 24-Jun-2020].
- [30] Ministerio de Salud, “Aprueban el Documento Técnico: Prevención , Diagnóstico y Tratamiento de personas afectadas por COVID-19 en el Perú,” 2020.
- [31] M. A. Suján, “Use of Ivermectin: Hope held out, caution called for,” The Daily Star, 2020.
- [32] M. Machicao, “Bolivian City Gives Out Free Doses of De-Worming Drug in Bid to Combat Coronavirus,” Reuters, 2020.
- [33] “Bolivian Region Authorizes Ivermectin as Treatment Against COVID-19,” Trial Site News, 2020.
- [34] R. Speare and D. Durrheim, “Mass treatment with Ivermectin: an underutilized public health strategy,” World Health Organization. [Online]. Available: <https://www.who.int/bulletin/volumes/82/8/editorial30804html/en/>. [Accessed: 24-Jun-2020].
- [35] <https://www.who.int/bulletin/volumes/82/8/editorial30804html/en/>
- [36] <https://www.givewell.org/international/technical/programs/river-blindness>
- [37] <https://pubmed.ncbi.nlm.nih.gov/21734116/>
- [38] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6159570/>
- [39] http://timesofindia.indiatimes.com/articleshow/76114654.cms?utm_source=contentofinterest&utm_medium=text&utm_campaign=cppst
- [40] <http://ctri.nic.in/Clinicaltrials/advsearch.php>
- [41] <https://m.indiamart.com/>
- [42] <https://www.lybrate.com/?lpt=NAV>
- [43] <https://www.medlineindia.com/antibiotic/Ivermectin.htm>
- [44] <https://www.1mg.com/>
- [45] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7253113/>



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