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Standards and urgency in times of pandemics: hydroxychloroquine as a pharmaceutical and political artefact

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By Manuel Campinas

Separated by two meters of water from the crowd, Brazil's President Jair Bolsonaro, infected by COVID-19 and wearing his mask, rallied up his supporters, "If by chance your mother or grandfather catches it, will they take chloroquine or not?"

"They will!" shouted back the crowd in unison, across the narrow strip of water.

Hydroxychloroquine has turned from being a commonly used antimalarial to becoming arguably the most political pharmaceutical in history (Giles, 2020). Referred to interchangeably by its name and as "chloroquine" by the Brazilian president, and at times simply as "hydroxy" by United States President Donald Trump, the medicine has been taken by both. The first did so to treat COVID-19, the second to prevent it. By promoting it since March 2020, hydroxychloroquine has afforded them political leverage, at least with their supporters, in extremely difficult pandemic times. The urgent need for solutions made them respond, in the populist mode that got them elected, by offering their "best evidence": that of having taken hydroxychloroquine themselves while attesting to its positive results. Such firsthand accounts, used to promote the use of hydroxychloroquine to millions, ignore the privilege of being closely monitored by their personal physicians in countries pervaded with inequities in the access to healthcare (Barbosa and Cookson, 2019; Paredes et al, 2020), even as they purport to be close to their electorate. The support for hydroxychloroquine by the two presidents has been visible in press conferences, an outdoor advert (Figure 1), as well as in social media. In regard to the latter, Trump's repost of a video by a group called "America's Frontline Doctors" hailing hydroxychloroquine as both prevention and a cure that dispenses with the need for lockdowns and masks, was removed by Twitter. The same video was taken down by YouTube and Facebook, with all three social media giants claiming it violated misinformation policies on COVID-19. President Trump, in turn, accused the companies of censorship.

Figure 1: Outdoor poster with President Bolsonaro next to a generic pack of hydroxychloroquine sulphate. The text reads "COVID-19 Early treatment saves lives!!" (Soares and Valfré, 2020)

In order to situate how hydroxychloroquine came to feature so prominently in debates on freedom of speech and of medical practice, as well as on misinformation, I will now step back to follow its path in becoming a political artefact. This January, before the less toxic hydroxychloroquine was taken up in COVID-19 clinical trials, chloroquine's reportedly promising in vitro results led Chinese researchers at the Wuhan Institute of Virology to select it for clinical trials (Xing, 2020). The following month, a number of quickly conducted clinical trials in China (Gao et al, 2020) were hailed in France as showing "Chloroquine and hydroxychloroquine as available weapons to fight COVID-19" (Colson et al, 2020), indicating hydroxychloroquine as the drug of choice between the two. Through social media, this report went on to ignite widespread enthusiasm with hydroxychloroquine in the US and beyond (Samuels and Kelly, 2020). Early in March, chloroquine already featured in China's "Diagnosis and

Treatment Protocol for Novel Coronavirus Pneumonia" (National Health Commission, 2020), and on March 16, the same French team issued a preprint with the results of their own clinical trial, which was peer-reviewed and accepted in 24 hours. This study confirmed their optimism towards hydroxychloroquine (Gautret et al, 2020), and the publication went on to be widely cited.

Two days later, Trump made his first mention of hydroxychloroquine referring to it as showing "very encouraging early results" and claiming it had already been approved by the FDA (which did not happen until the 28th, under an emergency use authorisation (Lenzer, 2020)). However, the journal's International Society of Antimicrobial Chemotherapy later released a statement remarking that "the article does not meet the Society's expected standard" (ISAC, 2020). Moreover, the trial on which the paper is based was then accused of having "several major methodological issues" (Machiels et al, 2020, p.1).

I argue that it is this tension between standards of research and urgency in times of pandemics that has made hydroxychloroquine deeply political. In order to understand this tension better, it is necessary to look into the WHO's shifting position on both hydroxychloroquine and chloroquine. Prior to the Chinese chloroquine clinical trials, in its "novel Coronavirus outline of trial designs for experimental therapeutics," the WHO stated that "there is insufficient evidence to support its further investigation" (WHO, 2020a, p.4). However, WHO's position changed by mid-March. While acknowledging that chloroquine's randomised controlled trials (RCTs) for antiviral activity in humans had been largely disappointing, the WHO used chloroquine's reported in vitro activity against SARS-CoV-2 (the virus responsible for COVID-19), as well China's ongoing chloroquine treatment studies, to justify that "there is equipoise for the inclusion of chloroquine in clinical trials and to proceed with the evaluation of chloroquine in COVID 19 patients" (WHO, 2020b, p.10). This shift was also a matter of convenience, since the WHO considered it preferable to receive the data from the more than 20 chloroquine studies taking place in China, rather than waiting for animal studies from the NIH (National Institutes of Health) (*Ibid.*). The relationship with China on this matter was not exactly fluid, since at the time, there had been no data sharing from China on chloroquine studies, despite assurances that collaboration would improve (*Ibid.*).

The WHO then went on to create the Solidarity trial (WHO, 2020c) that involved several countries and included a hydroxychloroquine arm. This arm lasted for about two months before it was interrupted (Mahase, 2020), following a massive study published by *The Lancet* that showed an increased mortality risk for those COVID-19 hospitalised patients on hydroxychloroquine (Mehra et al, 2020a). The plot then thickened, when

the said paper was retracted, following concerns regarding the validity of primary data sources (Mehra et al, 2020b), in what became known as the "Surgisphere scandal" (Servick and Enserink, 2020). WHO's hydroxychloroquine studies resumed in early June, only to come to a final halt two weeks later for hospitalised patients, citing evidence from the Solidarity trial and the UK's Recovery trial which pointed out that hydroxychloroquine did not reduce mortality (WHO, 2020d). Two days prior to this halt, the FDA had revoked its emergency use authorization for hydroxychloroquine and chloroquine (USFDA, 2020).

Amidst all this controversy, interest, and rejection of hydroxychloroquine for hospitalised patients, clinical trials continue to this date for COVID-19 pre and post-exposure prophylaxis (Giles, 2020; WHO, 2020d). Despite the WHO's "Clinical management of COVID-19" advising against using hydroxychloroquine or chloroquine in the treatment and prophylaxis of COVID-19 (WHO, 2020e) outside the context of clinical trials (for the risk of arrhythmia), it is for early treatment and prophylaxis that hydroxychloroquine found its most vocal supporters such as Trump and Bolsonaro. Arguably, hydroxychloroquine is political too in the likely interest in disproving its devoted medical recommendation from a man who suggested that "light inside the body" or disinfectant injection could be solutions to COVID-19 (Yamey and Gonsalves,2020). The worry that the drug is being discarded too early has been raised by UK scientists working on COVID-19 prophylaxis who now struggle to find study participants (Giles, 2020). This has taken place after the UK spent £3.5m to stock up on hydroxychloroquine and chloroquine (O'Carroll, 2020), at a time when the WHO clinical trials were in full swing.

The sense of urgency, and lack of mobilisation for large RCTs on hydroxychloroquine prophylaxis and early treatment, has brought to the surface issues of standards in research in the academic and medical world. More specifically, it has led a Yale epidemiologist to vouch for controversial studies such as that by Gautret et al (2020) as "the best that we have available" (Risch, 2020a, p.20), in his support for hydroxychloroquine early outpatient treatment. In the bitter replies to his paper, interestingly, the accusations were not so much directed at his main argument: that one should put in practice results from observational studies immediately until RCTs are completed. On the contrary, they were levelled at the many faults in the studies he cited as well as at the conclusions that he derived from these (Fleury, 2020; Korman, 2020; Peiffer-Smadja and Costagliola, D., 2020). In fact, there are plenty of criticism of RCTs in the medical field, while demonstrating the importance of observational studies (Gregor and Giordano, 2016; Glasziou et al, 2007; Collins et al, 2020; Frieden, 2017). Also, in anthropology, RCTs have been shown to present limitations and generalisability issues (Harper, 2006), disregard experiential aspects of healing (Barry, 2006), are generally

reductionist (Thompson et al, 2009) and have even been accused of constituting “Randomised Controlled Crime” (Adams, 2002). Therefore, it is not a case for those of us working on ethnographic research to point the finger at those whose sample size is not “large enough” or who avoid randomisation, but rather to analyse specific academic outputs for their own value and suitability for practical applications.

Apart from hydroxychloroquine, and in a less heated way, COVID-19 is bringing out other political pharmaceuticals. In China, where hydroxychloroquine and chloroquine COVID-19 trials first started, Chinese medicines (marketed abroad as TCM) are reportedly “bringing new hope for the prevention and control of COVID-19” (Ren et al, 2020, p.1), a claim backed by “thousands of years of experience in regulating the body and enhancing the resistance to epidemic diseases” (*Ibid.*, p.2). Indeed, several oral and injectable Chinese proprietary medicines as well as Chinese medicine decoctions have already made it to the “Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia” (National Health Commission, 2020). In my own fieldwork, I have reported on a complex political and marketising dimension of Chinese medicines (Campinas, forthcoming), which is only bound to grow more intricate in these pandemic times.

Back in the US and Brazil[1], with less pluralism at the state healthcare level and with stricter public health procedural guidelines, hydroxychloroquine has found political leaders who thrive by defying the status quo. In this way, hydroxychloroquine has played well into their way of doing politics, which derives authority from being above protocol. Such a stance, coupled with pandemic urgency, afford a perfect combination for their show of strength and resoluteness as Trump and Bolsonaro continue to promote hydroxychloroquine for early COVID-19 treatment.

In his *Newsweek* opinion piece “The Key to Defeating COVID-19 Already Exists. We Need to Start Using It,” Prof. Risch (2020b), the Yale epidemiologist, defends hydroxychloroquine use in COVID-19 and laments that it has become a “marker of political identity.” He ends his piece by suggesting that, in the future, sociologists of medicine will study this episode as a “classic example of how extrascientific factors overrode clear-cut medical evidence” (*Ibid.*). As a medical anthropologist, I argue that the “clear-cut medical evidence” that Prof. Risch refers to has itself been produced under rushed pandemic circumstances. These are the same circumstances that turned hydroxychloroquine into a political artefact. Thus, this medicine gained centre stage in polarised political climates desperate for solutions to an unforeseen, unprecedented public health challenge.

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anthropologist specialising in the anthropology of pharmaceuticals. He is currently a doctoral candidate at the London School of Hygiene and Tropical Medicine. His ethnographic research focuses on the industrialisation of "ethnic minority medicine" in China and he has previously conducted fieldwork in Siberia on "folk medicine" and post-Soviet transformations. He is also a member of the Anthropology of Antimicrobial Resistance Research Group at LSHTM.

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[1] For the pharmaceutical controversy over a cancer drug developed in Brazil, see Vilar, 2020.

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