Materials & Biomaterials Science
Researche and Engineering

Mater. Biomater. Sci. 04 (2021) 100–105
View Journal | View Issue

SHORT COMMUNICATION

Impact of Chloroquine as treatment of pandemic COVID-19 on environment

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ARTICLE INFO

Article history:
Received: 01 June 2021
Revised: 12 July 2021
Accepted: 20 July 2021
Published:04 August 2021

Keywords:
Covid-19
Hydroxychloroquine
Chloroquine
Pollution
Environment
Wastewater

ABSTRACT

The coronavirus disease 2019 (COVID-19) virus has spread rapidly as a pandemic public health concern. Until now, scientists have searched to discover drugs for its efficacious treatment to prevent or treat the disease of the pandemic COVID-19. Due to the rapid emergence of the pandemic in all geographic, unavailable of vaccine, clinical presentation and specific diagnostic tests imaginable challenges are proposed to combat this epidemic. Hydroxychloroquine and similar medication called Chloroquine, are shown to have apparent efficacy and acceptable safety against coronas virus wich were recommended as a treatment protocol of COVID-19 pandemic until a vaccine for COVID-19 is available but since Hydroxychloroqione HCQ and its metabolites reach wastewater treatment plant and environment where its occurence is a source of pollution and are identified as potentially persistent and bioaccumulative, behavior in the environment. Both chloroquine and hydroxychloroquine posed serious chronic threat to the aquatic organism. This is highly relevant since it is known that wastewater treatment systems do not have adequate processes for treatment these drugs, which will enter into freshwater ecosystems.

Introduction

Human activities release high levels of toxic pollutants from multiple sources around the globe, were contaminated the Earth [50]. However, different environments are daily exposed to these emerging pollutants, such as pharmaceuticals and their residues, from various sources; hospital and municipal wastewater, consumer use, or disposal and discharges from pharmaceutical production [17]. These products added to the list of priority substances by the Water Framework Directive of the European Union Decision 2015/495 as an emergence contaminant [35]. After use, their disposal unmetabolized are excreted by humans and due to their incomplete elimination in wastewater, a large part of drugs has been discharged into the environment. Now, Pharmaceutical contaminants (PhACs) appear broadly in the geosphere [65] and biosphere [7]. They have been detected in many aquatic bodies systems including drinking water supplies, groundwater and surface water [8,79], rivers [36], lakes [73], wastewater [32] effluent and influents, and sludge [23] ; also, soils and sediments [39] are contaminated by them. However, Due to their lipophilic property and their resistance to degradation, they persist in the aquatic environment where they present a serious issue throughout the world and have negative effects on the biota [4].

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Recently, in 2020 a new virus knows as SARS-CoV-2 (Coronavirus) invades and emerges the world via a widespread human transmission [5]. Since December 2019, the spread of Pandemic COVID-19 worldwide [12] as an infectious disease occurs after infecting a human with severe acute respiratory syndrome-related coronavirus (SARS-CoV-2) (ARDS). On January 31, 2020, COVID-19 as a Public Health Emergency of International Concern (PHEIC), was declared by WHO [41], however, that it can pose a menace to many countries and needs an urgent, coordinated international response [24]. On 11th March 2020, the WHO (2020) announced that the COVID-19 outbreak was a “pandemic public health menace.” For this, the necessity for early detection, quarantine, and rapid treatment was proposed by The global emergency committee [33].

Research in vitro and in vivo studies revealed that Chloroquine and hydroxychloroquine were highly effective against COVID-19 [27-43]. They were found that Chloroquine can block COVID-19 infection at low-micromolar concentration, with a half-maximal effective concentration (EC50) of 1.13 µM and a half-cytotoxic concentration (EC50) greater than 100 µM [49]. For this reason, national and international medical organizations over the world allowed certain hospitalized, to use chloroquine (CQ) and hydroxychloroquine (HCQ) as a treatment for patients contaminated by Coronavirus (COVID- 19) [21–7]. These substances are belong the quinoline group $C_{18}H_{26}ClN_3$ as molecular formula, CQ includes derivate products like Chloroquine phosphate ($C_{18}H_{29}ClN_3.H_3PO_4$), Chloroquine diphosphate ($C_{18}H_{29}ClN_3.2H_3PO_4$), Chloroquine sulfate ($C_{18}H_{26}ClN_3$. H_2SO_4) and Chloroquine dihydrochloride ($C_{18}H_{26}ClN_3$.2HCl) [31]. Since the 1930s, CQ has been used as Malaria treatment, due to its tolerability, effectiveness and inexpensive synthesis [15], also as an antifungal [32], treatment of rheumatic and immune-mediated diseases [35] and it is used also for the management of HIV, SARS-CoV and influenza A/H5N1 virus [36].But, Overproduction and overuse use of CQ and HCQ may entre the aquatic ecosystem via wastewater effluents, washing out of fecal materials by rain, domestic wastewater and STPs.

For this matter, it is better to understand the fate and behavior of HCQ and CQ in water matrices.

Effect of Chloroquine on Covid-19

For viral life cycles, the virus use the machinery and intracellular environment of a host cell, there are several other likely targets critical for RNA duplication, transcription or budding (Schoeman and Fielding, 2019. New research has proposed that hydroxychloroquine alters the glycosylation of the cellular receptors of coronaviruses [55]. However, the SARS-CoV-2 enters cells via receptor by inhibition tof angiotensin-converting enzyme 2 (ACE- 2) used by the virus for entry into the cell [57,58].In addition, hypothesis of scientists suggest that CQ/HCQ may exhibit reaction on coronavirus via two different mechanisms: immunity modulation and pH elevation of endosomes/lysosomes (Figure 1A,B) [53].
Chloroquine can incorporate into endosomes and lysosomes, resulting in an increased pH of intracellular compartments, this increase in pH results in their altering protein degradation pathways through acidic hydrolases in the lysosomes, macromolecule synthesis in the endosomes, and post-translational protein modification in the Golgi apparatus, endocytosis, and exocytosis needed for viral infection, replication, and propagation [56]. In addition, hydroxychloroquine has a modulating effect on activated immune cells,by a non-specific anti-inflammatory action (inhibition of interleukin-6 [IL-6],downregulates the expression of Toll-like receptors (TLRs) and TLR-mediated signal transduction [6] .

Presence and fate of Chloroquine and Hydroxydchloroquine in wastewater

Chloroquine and quinine are the derivatives of Quinoline, they are used for treatment of malaria desease. Also, they have used widely in Asia, Africa and South America for other medical treatment [1 ,22]. Substantial portion of Hydroxychloroquine excreted unchanged [8]. As a result, unchanged or metabolized part discharged from bodies via kidney (40–60%) and from feces (8–25%) as N-desethyl chloroquine,

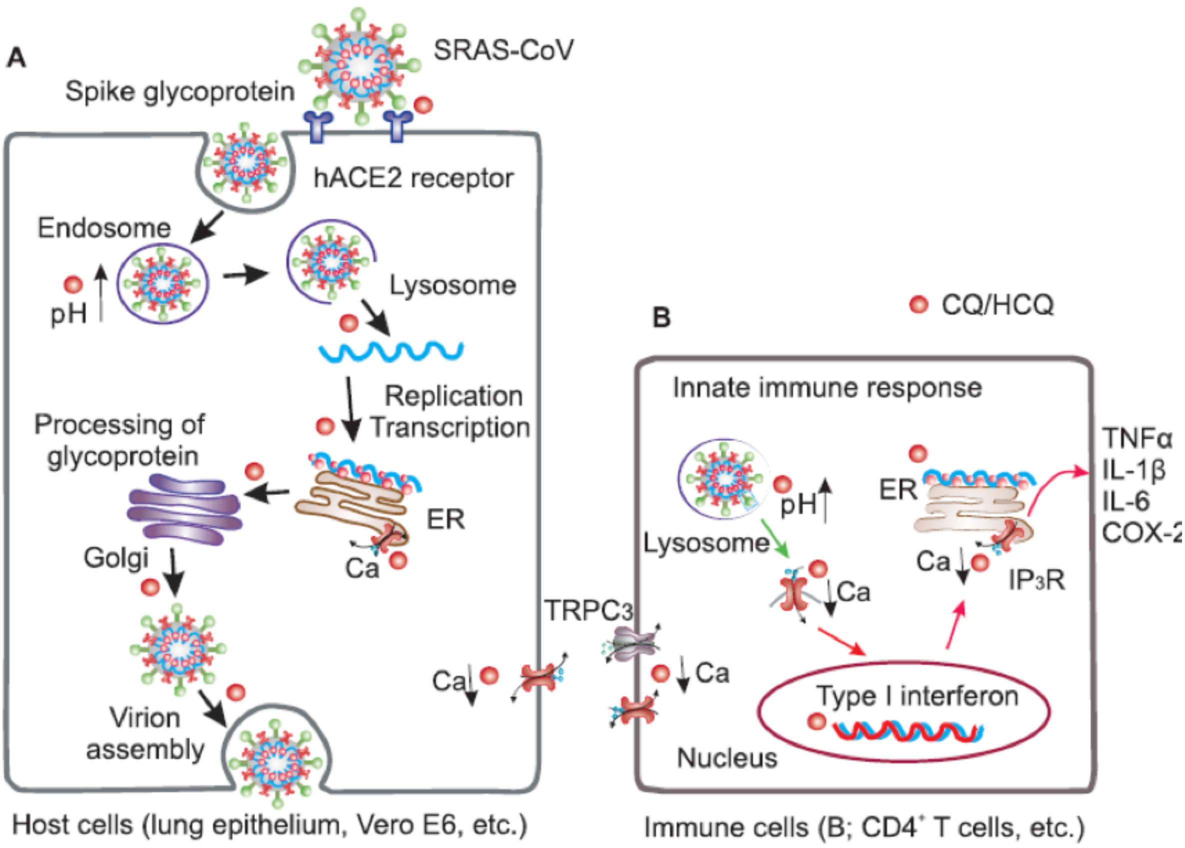

Fig. 1. Highlights of SARRS-CoV-2 lifecycle and proposed mechanisms of CQ/HCQ interruption of virulence: 1) modulation of endosome or lysosome function by elevation of pH, thereby nterrupting virus entry, as acidic pH is required for glycosyltransferases to modify envelope glycoprotein. CQ/HCQ impairs viral spike proteins binding with ACE2 receptors, thereby blocking virus-host cell fusion; Note that solid black arrows indicate the critical phases by which CQ/HCQ may disrupt the lifecycle of coronavirus (A). 2) Modulation of cytokine production (TNFα, etc.) and antigen presentation. The typical innate response to SARS-CoV-2 is marked by type I interferon. The anti-inflammatory property is proved effective for rheumatoid arthritis and lupus (B); 3) Intervention of intracellular calcium gradients, impairing RNA replication, spike glycoprotein production, and innate inflammatory response. Alternatively, attenuation of Ca2þ influx through viroporin (Green arrow) to mediate proinflammation (B). ER. Endoplasmic reticulum; hACE2, human angiotensin-converting enzyme 2; TNFα, tumor necrosis factor α [59].

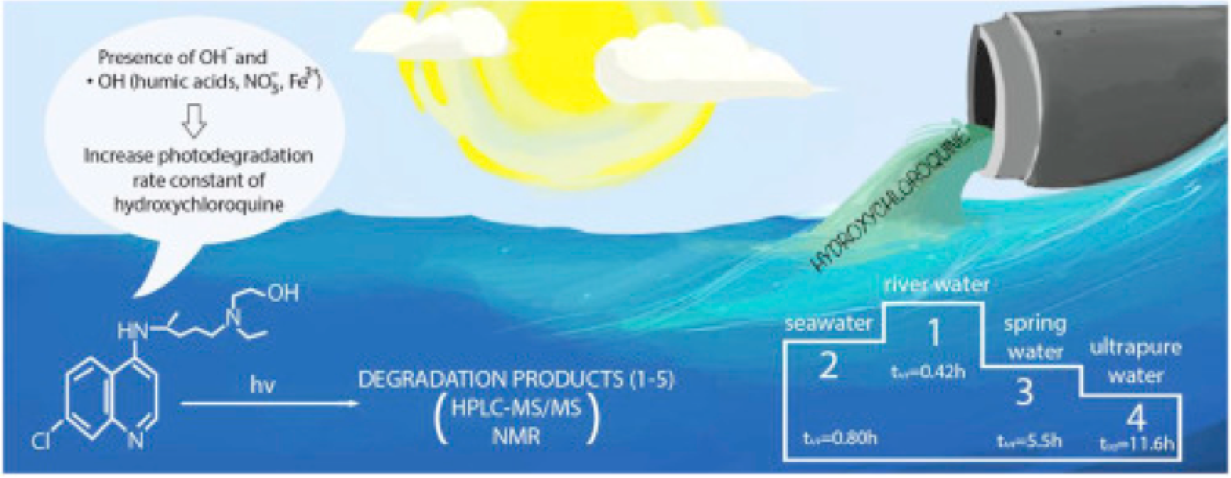

Fig. 1. Fate of Hydroxychloroquine in water bodies [8].

and quinine unaltered or as 3-hydroxyquinine [18; 23]. In addition, high levels of these drugs were discharged from hospital wastewater as first source and one would expect that their concentrations and diversity have increased during the COVID-19 pandemic due to a higher use [10;14;22]. As result, hydroxychloroquine was certainly fate of large quantities via wastewaters contaminated the environment. But just many studies can be found in the literature related to the degradation and fate of HCQ in water [8, 16,40].

Since hydroxychloroquine are identified as high volume production pharmaceutical, potentially persistent and bioaccumulative, understanding of its environmental fate and behavior is an important issue. Due to the fact that HCQ is potentially persistent and bioaccumulative and produced in large quantities, it has a high potential for being the next emerging pharmaceutical contaminant [9,17].

CQ and its metabolites reach wastewater treatment plants and they can be discharged into the environment where their fate and behavior are related by their physicochemical properties. At the wastewater treatment plants (WWTPs), a series of treatment processes are used to eliminate these compounds but due to inadequate treatment, these drugs enter into the aquatic environment. However, the abiotic degradation of HCQ in pure and natural waters by sunlight photolysis was investigated by Dabic et al. [8].

The photodegradation under solar irradiation could be an important elimination process for hydroxychloroquine in the environment. However, Both High-performance liquid chromatography- mass spectrometry (HPLC-MS/MS) and Nuclear magnetic resonance (NMR) spectroscopy confirm the degradation of HCQ into simpler molecules by photodegradation [8]; On the contrary, it has been demonstrated that HCQ is resistant to hydrolytic degradation. Mostly, some studies have been focused on the photochemical stability of HCQ in aqueous solution and none of them investigated its removal from aqueous solution.

As same as, the biotic degradation test of Hydroxychloroquine showed 0% degradation in 28 days [37]. So, Hydroxychloroquine is potentially persistent and bioaccumulate [39]. However, due to the large production of HCQ and its potentiality of persistence and bioaccumulation, it has a high potential for being the next emerging pharmaceutical contaminant [8, 9, 10)]. However, the degradation products themselves can pause substantial environmental concerns due to their high toxicity and bioresistance [26]. Therefore, the search for an effective method to eliminate this micropollutant from wastewater before its discharge in natural water bodies is needed to minimize its hazardous effects.

Although these drugs are persistent, bioaccumulative, and dangerous to aquatic organisms [24], This is highly relevant since it is known that wastewater treatment systems do not have adequate processes for treatment of these drugs, which will enter into freshwater ecosystems [2] (Fig. 2).

Despite the limited knowledge of the fate of antimalarial drug residuals in the environment, some studies detected these drugs residuals in many bodies. Even so, recently, in pharmaceutical industrial Sango-Ota, besides other pharmaceuticals (analgesics and antibiotics), Chloroquine was detected in wastewater where a concentration of 5.01 µg/L of Chloroquine was detected while those of Paracetamol, Ciprofloxacine and Diclofenac were 2.57 µg/L, 0.86 µg/L and 17.25 µg/L respectively [20]. Although, the result of Chen [6] in southeast China detected HCQ in surface sediment from tidal sections of the river.

Table 1 : Median effective concentration (EC50) of some organisme to CQ for 48h [42].

Test biota	Species	Effect of Chloroquine : EC50 (mg/L)
Fish	Poeciliopsis lucida	9
invertebrat	Daphnia magna	27
Micro-algue	Chlorella vulgaris	43
bacteria	Vibrio fischeri	126

Table 2 : Predicted No Effect Concentration (PNEC) by Protocol: (OECD 201).

Pharmaceutical product	Test biota	EC10 72h	EC50 72h	NOEC 72h	Ref.
Hydroxychloroquine	Algae (Pseudokirchneriella subcapitata)	1830 µg/L	3110 µg/L	768 µg/L	[24]
Hydroxychloroquine Sulfate	Algae (Pseudokirchneriella subcapitata)	1950 µg/L	3570 µg/L	183 µg/L	[25]

Table 3. Predicted No Effect Concentration (PNEC) by Protocol: (OECD 202 , 211).

	Test biota	EC10 48h	EC50 48h	NOEC 48h	Ref.
Hydroxychloroquine	Crustacean (Daphnia magna)	ND	14000 µg/L	6760 µg/L	[24]
	Test biota	EC10 21d	EC50 21d	NOEC 21d	Ref.
Hydroxychloroquine Sulfate	Crustacean (Daphnia magna)	173 µg/L	ND	85.8 µg/L	[25]

OECD :Organization for Economic Co-operation and Development, Guidelines for the Testing of Chemicals.

Also, chloroquine is likely to be absorbed by soil, however, a monitoring study of Miyai [17]. In the Japan, it's reported that the antimalarial drugs such as Chloroquine, Artesunate, Quinine, and Deoxycline are detected in a pharmaceutically polluted agricultural soil, their chlorinate carbon groups indicate some persistence. Although, Choloriquine with high concentrations are toxic to soybean and reduce the protozoa population of soil microbiota [14].

Ecotoxicity of Chloroquine and Hydroxydchloroquine

These drugs belong to a group of quinolone derivatives, which are recalcitrant, persistent, toxic, carcinogenic and teratogenic in nature. Both chloroquine and hydroxychloroquine posed serious chronic threat to the aquatic environment.

HCQ has high potential to persist, bioaccumulate, and transfer to living organisms in intensified toxic forms due to its chemical and biological properties [12,16]. It can also contaminate soil (bioaccumation in vegetation) [46,17], air (ozone depleting substance) [18] and groundwater (persistent substance) [17,6]. due to the large production and utilization of HCQ, it causes a high risks of natural water contamination [17,9, 50] wich necessitates more attention to limit its hazardous effects on human health and environment.

Predicted No Effect Concentration (PNEC) was PEC/PNEC ≤ 0.1: the use of HCQ has been considered to result in insignificant environmental risk (Table 2,3).

The expose of some organisms as fish cells and microorganism to CQ for 48h, the median effective concentration (EC50) was determibate in table 1. However, bioassays using the invertebrate Daphnia magna and alga Chlorella vulgaris suggested that chloroquine may be harmful to aquatic organisms [42]. In addition of binding of CQ with DNA and inhibits the metabolic functions, interfere with hemoglobin, it causes also cell mediated death [35].

As same as the findings of MacPhee and Ruelle [16] observed that the expose of salmon upon to 20 µM of CQ, caused mortality of fish, whereas only behavioral changes were noticed in rainbow trout exposed to 388 µM of CQ after 24 h [34].

Conclusion

There is limited information available on the potential environmental effects of chloroquine (CQ), But, the presence of Chloroquine and hydroxychloroquine residual drugs in the wastewater samples may constitute a significant environmental problem if allowed to persist for a while. Hence, inadequate water treatment plants and worse implementation of methodologies that contribute to decrease/elimination of these pharmaceuticals from water and wastewater is considered as high potential for being the next emerging pharmaceutical contaminant in World. So, it’s very important that the Researchers must currently be looking for depollute large quantities of wastewaters contaminated with HCQ drug and its metabolites especially this drug is adopted as the first treatment of COVID-19 by many health organizations.

References

1. Achan J, Talisuna AO, Erhart A, Yeka A, Tibenderana JK, Baliraine FN, D’Alessandro U, (2011). Quinine, an old anti-malarial drug in a modern world: role in the treatment of malaria. Malaria J. 10:144.
2. Ashfaq, M., Khan, K.N., Rehman, M.S.U, (2017). Ecological risk assessment of pharmaceuticals in the receiving environment of pharmaceutical wastewater in Pakistan. Ecotoxicol. Environ. Saf. 136, 31–39.
3. Bradley, PM, Battaglin, WA, Clark, JM, Henning, FP, Hladik, ML, Iwanowicz, LR, Journey, CA, Riley, JW and Romanok, KM, (2017). "Widespread occurrence and potential for biodegradation of bioactive contaminants in Congaree National Park, USA". Environ Toxicol Chem 36(11): 3045-3056.
4. Brandão, S. Rodrigues, B.B. Castroa, F. Gonçalves, S.C. Antunes, B. Nunes, (2013) . Short-term effects of neuroactive pharmaceutical drugs on a fish species: biochemical and behavioural effects Aquat. Toxicol., 144–145, pp. 218-229.
5. Bukhari, Q., Jameel, Y., (2020). Will Coronavirus Pandemic Diminish by Summer? (Available SSRN 3556998.
6. Chen J.S., Yu S., Hong Y.W., Lin Q.Y. and Li H.B, (2013). Pharmaceutical residues in tidal surface sediments of three rivers in southeastern China at detectable and measurable levels, Environmental Science and Pollution Research, 20, 8391–8403.
7. Christou, A.; Karaolia, P.; Hapeshi, E.; Michael, C.; Fatta-Kassinos, D, (2017). Long-Term Wastewater Irrigation of Vegetables in Real Agricultural Systems: Concentration of Pharmaceuticals in Soil, Uptake and Bioaccumulation in Tomato Fruits and Human Health Risk Assessment. Water Res. 109, 24–34.

8. DarioDabic, SandraBabic,IrenaŠkoriié ,(2019). The role of photodegradation in the environmental fate of hydroxychloroquine Chemosphere,Volume 230, September 2019, Pages 268-277.
9. Daughton C.G, (2014). The Matthew Effect and widely prescribed pharmaceuticals lacking environmental monitoring: Case study of an exposure-assessment vulnerability, Science of the Total Environment, 466–467, 315–325.
10. Dong L, Hu S, Gao J, (2020). Discovering drugs to treat coronavirus disease 2019 (COVID–19). Drug Discov Ther 14:58–60
11. EMEA/CHMP/SWP/4447/00 corr2, (2006). Guideline on the environmental risk assessment of medicinal products for human use, European Medicines Agency, Committee for Medicinal Products for Human Use, London.
12. Ebele A.J., Abou-Elwafa Abdallah M. & Harrad S, (2017). Pharmaceuticals and personal care products (PPCPs) in the freshwater aquatic environment. Emerging Contaminants 3: 1–16.
13. Escher, B.I., Baumgartner, R., Koller,M., Treyer, K., Lienert, J., McArdell, C.S.,(2011). Environmental toxicology and risk assessment of pharmaceuticals from hospital wastewater. Water Res. 45 (1), 75–92.
14. Gorbalenya A, Baker S, Baric R, (2020). The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nat Microbiol; 5: 536–544.
15. Grabicova, K, Grabic, R, Fedorova, G, Fick, J, Cerveny, D, Kolarova, J, Turek, J, Zlabek, V and Randak, T, (2017). "Bioaccumulation of psychoactive pharmaceuticals in fish in an effluent dominated stream". Water Res 124: 654-662.
16. Gosu, B.R. Gurjar, T.C. Zhang, R.Y. Surampalli, (2016). Oxidative degradation of quinoline using nanoscale zerovalent iron supported by granular activated Carbon, J. Environ. Eng.
17. Howard P.H. and Muir D.C.G, (2011), Identifying new persistent and bioaccumulative organics among chemicals in commerce II: Pharmaceuticals, Environmental Science and Technology, 45, 6938–6946.
18. Hossaini, M.P. Chipperfield, A. Saiz-Lopez, J.J. Harrison, R. Von Glasow, R. Sommariva, E. Atlas, M. Navarro, S.A. Montzka, W. Feng, S. Dhomse, C. Harth, J. Mühle, C. Lunder, S. O'Doherty, D. Young, S. Reimann, M.K. Vollmer, P.B. Krummel, P.F. Bernath, (2015).Growth in stratospheric chlorine from short-lived chemicals not controlled by the Montreal Protocol, Geophys. Res. Lett.
19. Jelic, A., Gros,M., Ginebreda, A, (2011). Occurrence, partition and removal of pharmaceuticals in sewage water and sludge during wastewater treatment. Water Res. 45 (3), 1165–1176.
20. Jjemba, P.K, (2002). The Effect of Chloroquine, Quinacrine, and Metronidazole on both Soybean Plants and SoilMicrobata. Chemosphere, 46, 1019–1025.
21. Li, S. Li, C. Bai, H. Liu, P, (2013).Gramatica, Structural requirements of 3-carboxyl- 4(1H)-quinolones as potential antimalarials from 2D and 3D QSAR analysis, J. Mol. Graph Model. 44.266–277.
22. MacPhee, R. Ruelle,(1969). Lethal effects of 1888 chemicals upon four species of fish from western North America, Wild l. Range Exp. Station Bull., No.3, University of Idaho Forest, Moscow, ID, p. 112.
23. Mahase, (2020).Covid-19: six million doses of hydroxychloroquine donated to US despite lack of evidence., BMJ.
24. Miyai, H., Hijikata, N., Kakimoto, T. & Funamizu, N, (2012). Determination Method for Antimalarial Drugs in Agricultural Soil Fertilized with Human Urine, Dry toilet conference 2012, Tampere Finland.
25. Mirghani RA, Ericsson O, Tybring G, Gustafsson LL, Bertilsson L, (2003). Quinine 3- hydroxylation as a biomarker reaction for the activity of CYP3A4 in man. European Journal of Clinical Pharmacology 59: 23-28.
26. Neuwoehner, A.K. Reineke, J. Hollender, A, (2009). Eisentraeger, Ecotoxicity of quinoline and hydroxylated derivatives and their occurrence in groundwater of a tarcontaminated field site, Ecotoxicol. Environ.
27. [OECD.Stat], OECD Statisics (2018). "Health/Pharmaceutical Market/Pharmaceutical consumption". Retrieved Aug 09, 2018, from https://stats.oecd.org/.
28. Olaitan, O. J., Anyakora, C., Bamiro, T., & Tella, A. T, (2014). Determination of pharmaceutical compounds in surface and underground water by solid phase extraction-liquid chromatography. Journal of Environmental Chemistry and Ecotoxicology. 6(3):20-26.
29. Ort, C., Lawrence, M.G., Reungoat, J., Eaglesham, G., Carter, S., Keller, J., (2010). Determining the fraction of pharmaceutical residues in wastewater originating from a hospital. Water Res. 44 (2), 605–615.
30. Price RN, von Seidlein L, Valecha N, Nosten F, Baird JK, White NJ, (2014). Global extent of chloroquine-resistant Plasmodium vivax: a systematic review and meta-analysis. Lancet Infectious Diseases 14: 982-99.
31. Projean D, Baune B, Farinotti R, Flinois JP, Beaune P, Taburet AM, Ducharme J , (2003). In vitro metabolism of chloroquine: identification of CYP2C8, CYP3A4, and CYP2D6 as the main isoforms catalyzing N-desethylchloroquine formation. Drug Metabolism and Disposition 31: 748-754.
32. Ramaswamy, G. Shanmugam, G. Velu, B. Rengarajan, D.G. Joakim Larsson,(2011). GC–MS analysis and ecotoxicological risk assessment of triclosan, carbamazepine and parabens in Indian rivers, J. Hazard. Mater. 186 (2–3)1586–1593.
33. Ramesh, M., Anitha, S., Poopal, R.K., Shobana, C., (2018). Evaluation of acute and sublethal effects of chloroquine (C18H26ClN3) on certain enzymological and histopathological biomarker responses of a freshwater fish Cyprinus carpio. Toxicol. Rep. 5, 18–27.
34. Rolain, J.M., Colson, P., Raoult, D., (2007). Recycling of chloroquine and its hydroxyl analogue to face bacterial, fungal and viral infections in the 21st century. Int. J. Antimicrob. Agents 30, 297–308. Sanofi internal report: Hydroxychloroquine Sulfate (CAS N° 747-36-4): Acute Toxicity to Zebrafish (Danio rerio) Embryos in a 96-hour Static Test. OECD 236. Report 127671238, July 2018.
35. Sanofi internal report, (2016). HYDROXYCHLOROQUINE (CAS N°118-42-3) DAPHNIA MAGNA, ACUTE IMMOBILISATION TEST. OECD 202. Report BPL15-0032 EDA. June 2016.
36. Sanofi Internal report, (2019). : Hydroxychloroquine Sulfate (CAS N° 747-36-4): Toxicity to Pseudokirchneriella subcapitata in an Algal Growth Inhibition Test. OECD 201. Report 135551210, March 2019.
37. Sanofi Internal report, (2019). Hydroxychloroquine Sul-

fate (CAS N° 747-36-4): Influence to Daphnia magna in a Semi-Static Reproduction Test. OECD 211. Report 135551221, February 2019.
38. Santos, A.N. Araujo, A. Fachini, A. Pena, C. Delerue-Matos, M.C. Montenegro,(2010). Ecotoxicological aspects related to the presence of pharmaceuticals in the aquatic environment, J. Hazard. Mater. 175 .45–95.
39. Saini, G. Bansal, (2013). Characterization of four new photodegradation products of hydroxychloroquine through LC-PDA, ESI-MSn and LC-MS-TOF studies, J. Pharm. Biomed. Anal.
40. Shen, N. Wu, Y. Wang, H. Zhao, L. Zhang, T. Li, M. Zhao,(2017). Chloroquine attenuates paraquat-induced lung injury in mice by altering inflammation, oxidative stress and fibrosis, Int. Immunopharmacol. 46 ,16–22.
41. Shinde, J.S. Raut, N.M. Chauhan, S.M. Karuppayil, Chloroquine sensitizes biofilms of Candida albicans to antifungal azoles, Braz. J. Infect. Dis. 17 (4) (2013) 395–400.
42. Sohrabi, C., Alsafi, Z., O'Neill, N, (2020). World health organization declares global emergency: a review of the 2019 novel coronavirus (COVID-19). Int. J. Surg. 76, 71–76.
43. Tojo, M.T. Santamarina, F.M. Ubeira, J. Leiro, M.L. Sanmartin,(1993). Efficacy of antiprotozoal drugs against gyrodactilosis in rainbow trout (Oncorhynchus mykiss), Bull. Eur. Assoc. Fish Pathol. 13.79–82.
44. Thomé, S.C.P. Lopes, F.T.M. Costa, L. Verinaud, (2013). Chloroquine Modes of action of an undervalued drug, Immunol. Lett. 153,50–57.
45. Takano, Y. Katoh, T. Doki, T. Hohdatsu, (2013).Effect of chloroquine on feline infectious peritonitis virus infection in vitro and in vivo, Antiviral. Res. 99,100–107.
46. Tonnesen H., Grislingaas A.L., Woo S.O. and Karlsen J. (1988), Photochemical stability of antimalarials. Hydroxychloroquine, International Journal of Pharmaceutics, 43, 215-219.
47. Tuo, J.B. Yan, B.A. Fan, Z.H. Yang, J.Z. Liu, (2012).Biodegradation characteristics and bioaugmentation potential of a novel quinoline-degrading strain of Bacillus sp. isolated from petroleum-contaminated soil, Bioresour. Technol.
48. Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, Shi Z, Hu Z, Zhong W, Xiao G. (2020).Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res.
49. Warhurst, D.C, (2003). Hydroxychloroquine is much less active against chloroquine-resistant Plasmodium falciparum, in agreement with its physicochemical properties. Journal of Antimicrobial Chemotherapy 52, 188 – 193.
50. World Health Organization, (2020). Coronavirus disease (COVID-19) outbreak. [cited 2020 April 2]. Available from: https://www.who.int/ emergencies/diseases/novel-coronavirus-2019.
51. World Health Organization, (2013). Middle East Respiratory Syndrome Coronavirus (MERSCoV). https://www.who.int/emergencies/mers-cov/en/, Accessed date: 5 February 2020
52. Zhang, R.A. Di Lorenzo, P.A. Helm, E.J. Reiner, P.H. Howard, D.C.G. Muir, J.G. Sled, K.J. Jobst,(2019). Compositional space: a guide for environmental chemists on the identification of persistent and bioaccumulative organics using mass spectrometry, Environ. Int
53. Zumla, A., Chan, J.F., Azhar, E.I., Hui, D.S., Yuen, K.Y., (2016). Coronaviruses – drug discovery and therapeutic options. Nat. Rev. Drug Discov. 15, 327–347.
54. Jorge AM, Melles RB, Zhang Y, Lu N, Rai SK, Young LH, et al.,(2018). Hydroxychloroquine prescription trends and predictors for excess dosing per recent ophthalmology guidelines. Arthritis Res Ther 20:133. doi: 10.1186/s13075- 018- 1634- 8.
55. Fantini J, Scala CD, Chahinian H, Yahi N.,(2020). Structural and molecular modeling studies reveal a new mechanism of action of chloroquine and hydroxychloroquine against SARS-CoV-2 infection. Int J Antimicrob Agents 105960.
56. Al-Bari MA.(2015). Chloroquine analogues in drug discovery: new directions of uses, mechanisms of actions and toxic manifestations from malaria to multifarious diseases. J Antimicrob Chemother; 70:1608–21.
57. Wan Y, Shang J, Graham R, Baric RS, Li F.,(2020).Receptor recognition by the novel coronavirus from Wuhan: An analysis based on decade-long structural studies of SARS coronavirus. J Virol 94: e00127-20.9.
58. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al.,(2020). A pneumonia outbreak associated with a new coronavirus of probablebat origin. Nature 579:270-3.
59. Zhan, X., Dowell, S., Shen, Y., & Lee, D. L. (2020). Chloroquine to fight COVID-19: A consideration of mechanisms and adverse effects?. Heliyon, e04900.

Conflicts of interest

Authors declare no conflict of interests.

Notes

The authors declare no competing financial interest.

Materials & Biomaterials Science

How to cite this article

S. Saim, B. Behira. Impact of Chloroquine as treatment of pandemic COVID-19 on environment. Materials and Biomaterials Science 04 (2021) 100-105.