Modern Chemistry & Applications

OPEN ACCESS Freely available online

Commentary

Why are Bat Molecules More Effective Than Chloroquine and its Derivatives Against The Covid-19 Epidemic? Opinions and Comments

Abdelkader Rahmouni[*1], Fatima Zohra Zeggai[1,2], Bachari Khaldoun[2], Redouane Chebout[2] and Mohammed Belbachir[1]

[1]Laboratory of polymer chemistry, Oran1 University Ahmed Benbella, BP 1524, El'Menouer, 31000 Oran, Algeria; [2]Centre de Recherche Scientifique et Technique en Analyses Physico-chimiques (CRAPC), BP 38Bou-Ismail-RP 42004, Tipaza, Algeria.

ABSTRACT

There is no doubt that the year 2020 remains an unforgettable era for all inhabitants of the earth due to the terrible Covid-19 outbreak and its consequences; this epidemic hasconfused scientists as they could not confront the challenge of its intelligence and decipher its code, especially within the cellwhich makes it a favorite space for its reproduction. In this paper, a design of drugs hasbeen proposed to improve the therapeutic effects of antiviral drugs, such as reducing drug resistance anddrug toxicityas well assolubility at room temperature.On the other hand,we have evaluated the therapeutic efficacy in the virology of the synthesized molecules, called Bat molecules, and compared it to that ofchloroquine.

Keywords: Covid-19; Nanomaterials; Drug delivery; Chloroquine; Virology; Bat molecules.

CASE REPORT

Chloroquine and its derivatives wereapproved in the late 1940s to treat malaria. Hydroxychloroquine, a derivative of chloroquine, is often used to treat rheumatoid arthritis and lupus [1]. Some doctors recommend the use ofthese drugs in a hope to reducethe duration of Covid-19 in their patients [2]. New results may create the hopethat the antimalarial drug can be used in thefight against coronavirus [3]. The undesirable effects of chloroquine are, however, numerous.Hence, somedistrust amongcertain doctors and scientists is created regarding its massive delivery to the patients suffering from Covid-19 before the end of the discovery test. The main side effects include: [4]:

• Digestive disorders with the following symptoms: nausea, vomiting, and diarrhea [5].

• Allergic reactions [6].

• Insomnia, depression, agitation, anxiety, aggression, sleep disorder, confusion, hallucination [2].

• Vision problems with blurred vision; also, rare cases of retinopathies linked to the molecular accumulation [3].

• Local pain, resembling burns, tingling, or electric shocks inthe hands and feet [7].

• Hypoglycemia (hence,the probabilityof rigor in diabetic patients) [8].

• Hepatobiliary disorders: hepatitis occurring in particular in patients with late skin porphyria [9].The data described in this paper is intended to providea new method for the synthesis of new antiviral molecules, called Bat molecules, especially for coronavirus (COVID-19), and to compare its features to the chemical, physical and biological properties of chloroquine molecule [10]. The bat molecules could overcome drug resistance,thereby suggestingthat the mechanism or phenomenonresponsible for resistance is highly selective and structurally specific. The anticoronavirus activity of the Bat molecule-resistant viral strains could only be due to a specific difference in the interaction with the resistance mechanisms of the virus.

EXPERIMENTAL DETAILS

Materials and methods

Potassium hydroxide (KOH), sodium hydroxide (NaOH), sodium carbonate (Na2CO3), potassium bicarbonate (KHCO3),nitric acid (HNO3), urea, orcinol, ethylene glycol, ethanol, hydrochloric acid (HCl) and potassium carbonate(K2CO3) wereall purchasedfrom SigmaAldrich.Prior to use, the materials were dried under vacuumat100°Cfor 2 minutes toremove residualwaterinthecrystals [11].The morphology and molecular structure of the samples were analyzed by using an X-ray fluorescence (XRF, Philips 1404 wavelength dispersive spectrometer) as well asaproton

Correspondence to: Arpan Gandhi, Dr Shroff's Charity Eye Hospital, India, Tel: +919810195021; E-mail: arpan.gandhi@sceh.net

Received: February 03, 2021; **Accepted:** February 20, 2021; **Published:** March 04, 2021

Citation: Rahmouni A, Zeggai FZ, Khaldoun B, Chebout R and Belbachir M. (2021) Why are bat molecules more effective than chloroquine and its derivatives against the Covid-19 epidemic? Opinions and comments. Mod Chem Appl. 9:278.

nuclear magnetic resonance)1HNMR). 1HNMR spectra wereobtained by applying a 300 MHz Advance Bruker spectrometerat room temperature using tetramethylsilane (TMS) and deuterated chloroform (CDCl3) as an internal standard and the deuterated solvent, respectively.In addition, a scanning electron microscope (LEO SEM 1450) was utilized to obtain SEM images. Infrared spectra (ATR absorption) were recorded on an Alpha Brucker spectrometer in the wavelength range of4000 to 400 cm□1 [12]

Synthesis of molecule

Molecule1 was formed throughthe condensation reaction between orcinol (2 g) and urea (2 g) in ionized water (20 mL). In this reaction, anucleophilic substitution could take place by the corresponding amine [13].This wascarried out in the presence of a molar ratio of diamine and orcine reagents, helping to avoid the formation of the terminally disubstituted diamine. After heating the mixture with the conventional method for 10 minutes, the process was continuedby dilution of carbonate potassium (1 M K2CO3) as the catalyst. Even though the reaction completion wasestimated, the yield wasdependent on the solubility of the products in water during the reaction process. After the solution reduction to a small volume, the products were precipitated by the addition of cold ethanol. The pure compound was characterized by 1H NMR as shown in (Figures 1)14].

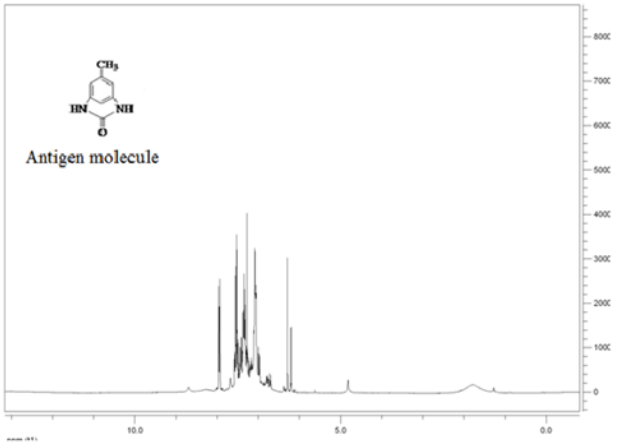

Figure 1: 1H NMR (CDCl3, 300 MHz) spectrum of the synthesized antigen molecule

The molecule called “Bat A”was prepared with slight modifications. Molecule 1 (0.05 g in 15 mL of ionized water) was added in a dropwise manner to a stirred solution of freshly distilled ethylene glycol (2 mL) in ionized water (5mL). NaOH (0.5g) as the catalyst was added to the mixture. The reaction mixture was stirred under inert atmosphere at 90°C for1 hour. The organic layer was separated and the aqueous layer was extracted with portions of cold ethanol (2 x 10 mL). The combined organic fractions were dried over anhydrous MgSO4. Then,the impurities were removed under the reduced pressure to afford a brown solid. The Bat A moleculewasa brown solid (1.78 g, yield 95.29%)with the chemical structure displayed in scheme (2).

CONCLUSION

There are many drug interactions with chloroquine-based drugs such as Nivaquine®which must be taken into account before prescription. There is also a need for close eye monitoring in the long-term patients. Regular monitoring of liver and kidney functions is,therefore,recommended. In addition, cardiac monitoring is necessary, regarding the co-prescription of chloroquine or hydroxychloroquine with Azithromycin to the patients with Sars-covid-2 (virus responsible for covid-19). Finally, chloroquine and its derivatives are so-called «narrow therapeutic margin» drugs, which means that the effective dose and the toxic dose are relatively close. In the case of overdose or improper use, they can behighly toxic. Bat molecule drugsinteract with the virus in a waydifferent from that of chloroquine.These new molecules present some advantages over the traditional chloroquine in anti-virology studies; it is safer to handle as it is non-toxic, it is soluble in water at room temperature, and its biological properties allow it to be monitored by the common equipment. Using microscopyplatform, we showed that the Bat molecules could interact with virus in a manner different from that ofchloroquine,whichis localized inthe digestive vacuole of the virus. Furthermore,the inhibited growth of chloroquine-sensitive strainsis more extensively in comparison tothe resistant strains against the bat molecules directly targeting the nucleus.We believe that the synthesizedmolecules could be valuable tools in the future drug discovery projects andso, they could be used in the treatment of virus, especially covid-19.

ACKNOWLEDGMENTS

This work,which was supported by the DGRSDT of Algeria, was carried out within the State Program of the second national forum.

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