Oxadiazoles for Covid-19?

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Oxadiazoles are a class of heterocyclic aromatic chemical compounds, having different isomeric forms. They appear in a variety of pharmaceutical drugs (among them the antiviral Raltegravir). Can these drugs have a possible role in the treatment of Covid-19? Or, why can't they be used for?

Torino 22 May 2020, DOI: 10.5281/zenodo.3841079

Several drugs are under investigation of clinical trials to find the best of them in the treatment of Covid-19 [1]. Some are used to reduce the cytokine storms, such as Tocilizumab, others are antivirals. In the case of Hydroxychloroquine, an antimalarial, it is used for its anti-inflammatory effect and also for a possible antiviral effect in patients of Covid-19.

However, some drugs exist, based on Oxadiazole compounds, which have antimalarial, anti-inflammatory and antiviral features. Then, here we want to pose a question: can Oxadiazoles have a possible role in the treatment of Covid-19?

Oxadiazoles are a class of heterocyclic aromatic chemical compounds, which are interesting also for their liquid crystalline phases [2]. In one of their isomeric forms, Oxadiazoles appear in a variety of pharmaceutical drugs. In particular, in [3] it is told that "compounds containing 1,3,4-Oxadiazole ring in their structure are characterised by multidirectional biological activity. Their anti-proliferative effects associated with various mechanisms, such as inhibition of growth factors, enzymes, kinases and others, deserve attention. ... In most publications, the most active derivatives of 1,3,4-Oxadiazole exceeded the effect of reference drugs, so they may become the main new anti-cancer drugs in the future". In fact, the "Oxadiazole isomers occur in the structure of many drugs, e.g., antitussive Oxolamine, antimicrobial Furamizole, antiviral Raltegravir and others" [3]. Moreover, it is also stressed that there "are numerous literature reports confirming the multidirectional effect of compounds containing the 1,3,4-oxadiazole ring in its structure". We find, among the others, antimalarial [4], anti-inflammatory [5] and antiviral effect [6,7] (see also [8,9]), besides anti-cancer properties.

Since Hydroxychloroquine is an antimalarial, and an antimalarial Oxadiazole compound exists, it could be interesting to test for this drug a possible effect on Sars-Cov-2. The same we can repeat for the Oxadiazoles having anti-inflammatory and antiviral properties.

The posed question (can these drugs have a possible role in the treatment of Covid-19?) is therefore reasonable. Alternatively, why can't Oxadiazoles be used for treatment?

A note on Raltegravir - 23 May 2020.

Raltegravir is an antiretroviral medication used, together with other medication, to treat HIV/AIDS. According to NIH, currently, there are 332 clinical trials about this drug (no one about Covid-19).

However, the following study exists, given in Ref. [10]. For the authors of the study entitled "Targeting SARS-CoV-2: a systematic drug repurposing approach to identify promising inhibitors against 3C-like proteinase and 2′-O-ribose methyltransferase", it was imperative "to identify promising inhibitors from pre-existing antiviral drugs". They have studied the two druggable targets mentioned in the tile. They have been selected "due to their indispensable nature in the viral life cycle". "The selected drug target proteins were screened against an in-house library of 123 antiviral drugs. Two promising drug molecules were identified for each protein based on their estimated free

energy of binding (ΔG), the orientation of drug molecules in the active site and the interacting residues. The selected protein-drug complexes were then subjected to MD simulation, which consists of various structural parameters to equivalently reflect their physiological state. From the virtual screening results, two drug molecules were selected for each drug target protein [Paritaprevir (ΔG = −9.8 kcal/mol) & Raltegravir (ΔG = −7.8 kcal/mol) for 3CLpro and Dolutegravir (ΔG = −9.4 kcal/mol) and Bictegravir (ΔG = −8.4 kcal/mol) for 2′-OMTase]. After the extensive computational analysis, [the authors] proposed that Raltegravir, Paritaprevir, Bictegravir and Dolutegravir are excellent lead candidates for these crucial proteins and they could become potential therapeutic drugs against SARS-CoV-2". Raltegravir is also considered in [11].

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