

# **Archives of Pharmacology and Therapeutics**

**Editorial** 

# Reflections on COVID-19 Pharmacological Treatment and Beyond: Beware of "Salads" with Many Ingredients but Low Scientific Content

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### **Editorial**

"Anyone can play in a strange way, that's easy. What's difficult is being as simple as Bach. Making the simple complicated is normal; making the complicated simple, terribly simple... That's creativity" (Charles Mingus, famous jazz bassist, composer and conductor, 1922-1979).

The pandemic triggered by SARS-CoV-2 has changed since that first case in Wuhan in 2019. We currently have efficient vaccines that have allowed us to return to our daily activities. But, SARS-CoV-2 remains a public health emergency of international concern. As soon as the pandemic began, the search was on for a drug that could prevent infection, or at least the worst consequences of infection. The rest of the story is known: It takes more than 15 minutes to list all the potential treatments for COVID-19, many of them unproven, with questionable results, with confusing, conflicting, low-quality evidence, including treatments for which data from randomized trials were not available, and also used at higher doses than usual, frequently in combinations of several of them and of course off-label and Over-the-Counter, both for prophylaxis and treatment [1,2].

Azithromycin, cloperastine, antihistamines, doxycycline, fluoroquinolones, ceftriaxone, hydroxychloroquine, ivermectin, fluvoxamine, metformin, sabizabulin, indomethacin, celecoxib, dipyridamole, fenofibrate, aprotinin, fluphenazine,

nimesulide, estradiol, famotidine, zinc, ursodeoxycholic acid, infliximab, abatacep, finerenone, colchicine, statins, aspirin, dimethyl fumarate, fluticasone, iminosugars, vitamins C, D, and E, l-lysine, 2-deoxy-D-glucose, nitric oxide, omega-3 fatty acid, ethyl-eicosapentaenoic acid, dexamethasone, ACE inhibitors and ARBs, dipeptidyl peptidase-4 inhibitors, baricitinib, remdesivir, favipiravir, baricitanib, bevacizumab, tocilizumab, lopinavir-ritonavir, interferon, sarilumab, ribavirin, nitazoxanide, umifenovir, niclosamide, abatacept, cenicriviroc, interleukin inhibitors, molnupiravir, nirmatrelvir/ritonavir, bamlanivimab, imbdevimab, casirivimab, among others were proposed and used. Cocktails such as methylprednisolone, ascorbic acid, thiamine and heparin, with additional therapies such as zinc, vitamin D and melatonin were also used. Some of these drugs and drug cocktails are still prescribed [3-7].

Is it a "salad" with more than 5 or 6 items? In gastronomy this is a trend that should be avoided. It is a useless and dangerous complication, because flavors are lost and masked, it is more expensive and difficult. The main ingredient is hidden and loses its flavor. When you are offered a salad with red cabbage, red onion, quail eggs, pistachios, almonds, a few drops of agar-agar, German gherkins, San Marzano tomatoes, sesame seeds, flax seeds, huacatay, fresh oregano, purple basil, black garlic, hazelnut oil, 11 year old Modena oil, Himalayan salt and whatever else you have on hand, switch restaurants. In medicine the tendency to polypharmacy must also be avoided.

The truth is that of these interventions, only one or a couple of them seem to have finally proven to be effective, although not without controversy in COVID-19:

- 1. Nirmatrelvir/ritonavir. It is recommended in non-hospitalized patients with mild to moderate disease and risk of developing severe disease. But its launch has been hampered by concerns about "rebound", side effects, drug interactions, inadequate funding for distribution, the high price of the drug, the need to take it soon after infection, and in some people certain foods taste bitter or metallic reinforcing the perception that it is toxic [8,9].
- 2. Remdesivir. It is recommended in non-hospitalized patients in the first days of illness who are at high risk of developing severe disease and in hospitalized patients for 5 days. But it must be administered intravenously in hospitals and has side effects in geriatric patients [10].
- 3. Other drugs are no longer recommended. Such as molnupiravir, that has ceased to be authorized due to lack of efficacy and adverse effects such as the possible induction of mutations in the viral genome [11-14]. Or the monoclonal antibodies in which the appearance of new viral variants affects their effectiveness; and the use of dexamethasone is recommended only in those hospitalized patients who require oxygen due to high-flow spikes or mechanical ventilation [15].

The pressure generated by the emergence of health events or situations for which there was no clear therapeutic approach is understandable. But it must not be forgotten that these bad interventions can cause damage to health [16-18]. In addition, the irrational use of auxiliary tests, including computed tomography and X-rays, only increases the anxiety of the patient and the doctor, who is often "forced" to prescribe a treatment directed at the complementary tests instead of clinical condition of patient [19].

The COVID-19 pandemic is putting biomedicine and health services focused on the biomedical approach in their place: it allows us to relocate the true importance of the drug (magical; useless, with serious effects adverse, with great economic interests, etc.) versus vaccination, public health measures, approaches focused on the social determinants of the disease and on preventive activities [20].

In reality, the culture of polypharmacy, the use of drugs in unapproved indications, the indiscriminate and unjustified use of drugs, as well as the prescription of higher doses than usual, was a practice prior to COVID-19, although the pandemic has been an ideal scenario to promote it even more. The crucial elements on which we believed the practice of medicine, especially general medicine, was based, such as the use of the clinical interview, continuity of care, knowledge of the context for diagnosis and treatment, wise use of drugs and technologies, as well as a permanent capacity to reflect critically on the situation that is presented in the consultation, seem to have disappeared a long time ago [21]. This polypharmacy "salad" with too many ingredients blocks the taste of the main component of medical care, the doctorpatient relationship [22]. It can be said that polypharmacy is

an indicator of medical malpractice and low quality of health care [23].

Obviously, it is very difficult, but it is necessary to make the complicated simple. As a character from the writer Raymond Chandler says in the Blue Dahlia "Don't complicate your life so much. When an individual makes it too complicated, he is miserable. And when he is unhappy, luck escapes."

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