BIOCHEMISTRY OF PAXLOVID

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Introduction. Since December 2019, the pandemic of coronavirus disease 2019 (COVID-19) has taken a heavy toll on global health, creating an urgent need to develop effective strategies for prevention and treatment. The etiological agent, known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has infected nearly 229.2 million people worldwide with more than 4.7 million deaths as of September 15, 2021. The global race to combat this pandemic has led to rapid deployment of numerous effective vaccines against SARS-CoV-2. However, the emergence of viral variants, including the Delta variant, compromised vaccine effectiveness with resurgence of SARS-CoV-2 infection among highly vaccinated population. Therefore, development of therapeutics against the more conserved viral targets would be essential to contain the spread of COVID-19 and reduce mortality. Pfizer has launched a study investigating an oral antiviral drug for the prevention of COVID-19 infection among individuals who have been exposed to the coronavirus.

Aim. The aim of the study was to collect the information about chemical structure and biochemical mechanisms of PF-07321332 effects, the first orally available Covid-19 clinical candidate, has recently been revealed by Pfizer.

Materials and methods. In order to achieve this goal, an information search was conducted in the materials of scientific articles.

Results and discussion. PF-07321332 is an antiviral drug developed by Pfizer which acts as an orally active protease inhibitor. The combination of PF-07321332 with ritonavir is in phase III trials for the treatment of COVID-19. PF-07321332: is designed to block SARS-CoV-2-3CL protease activity, also called Mpro. PF-07321332 inhibits viral replication at a stage known as proteolysis, which occurs before viral RNA replication. In the human cell, viral RNA synthesizes large or long proteins called polypeptides (pp1a and pp1ab) that will allow it to build the virus, including structural proteins. These polypeptides must be cut into small units to form the new viruses. An enzyme called protease is responsible for cutting these long polypeptides. Protease inhibitors like PF-07321332 bind to the protease to prevent (inhibit) its action. In preclinical studies, PF-07321332 did not demonstrate mutagenic interactions with DNA.

Conclusions. PF-07321332 inhibits viral replication at a stage known as proteolysis, which occurs before viral RNA replication. In preclinical studies, PF-07321332 did not demonstrate evidence of mutagenic DNA interactions.