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COVID-19: Artificial sputum, respiratory obstruction method and screening of pyolitic and antihypoxic drugs

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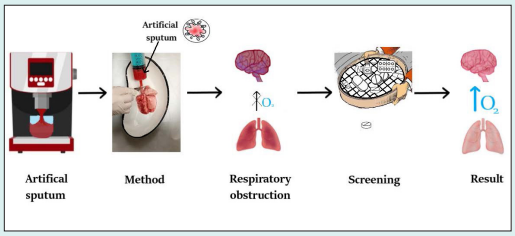
Abstract



COVID-19 causes non-specific pneumonia, which has become a new cause of hypoxia, leading to the death of many patients. Today, there are no effective drugs that provide an urgent increase in blood oxygenation. Therefore, it is urgently necessary to develop drugs to increase blood oxygenation in order to save the lives of patients with the new coronavirus infection. Since hypoxia develops in this disease due to the blockage of respiratory tract with viscous mucus and sputum, an appropriate experimental model is needed for screening and finding new drugs. However this model is yet missing. Therefore, the development of an experimental model of respiratory obstruction by sputum with traces of blood can accelerate the discovery of drugs that eliminate hypoxia and prevent the death of patients with nonspecific pneumonia complicated by respiratory obstruction. The purpose of this letter was to present a model for evaluating the biological activity of drugs, which can become a new vector for the development of effective ways to increase blood oxygenation across pulmonary and save the lives of patients with severe atypical pneumonia complicated by respiratory obstruction in COVID-19.

Dear Editor,

COVID-19 is a viral disease that causes atypical pneumonia, the severe stage of which is complicated by respiratory obstruction, which reduces blood oxygenation, causes hypoxia, hypoxic brain damage, and death of patients. Unfortunately, today there are no drugs that provide urgent elimination of respiratory obstruction and hypoxia, and there are also no relevant experimental models for screening. This situation hinders the search and development of new drugs, since the use of computational methods of docking has not yet reached perfection.[1,2]

One of the reasons for airway obstruction, which complicates the severe stage of SARS caused by the new coronavirus infection, is the excessive accumulation of viscous sputum in the airways.[3] Blockage of the respiratory tract with viscous sputum stops the delivery of oxygen to the alveoli.[4] This reduces the effectiveness of resuscitation with artificial ventilation of the lungs and allows to increase blood oxygenation only with the help of extracorporeal membrane oxygenation (ECMO). However, ECMO is not a safe and affordable method of providing emergency medical care. Therefore, it is urgently necessary to develop safe and affordable drugs that can immediately increase the oxygen content in the alveoli of the lungs and increase blood oxygen saturation. This will help save the life of almost every patient with severe hypoxia in any conditions.

It is no secret that the straight cause of irreversible brain's cell damage in patients with severe atypical pneumonia caused by COVID-19 is not the new coronavirus, but hypoxia. Therefore, the correct vector of developing new means and ways to save the lives of patients can only be directed to the immediate increase in blood oxygenation, but not to coronavirus. Since the reason for the cessation

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of oxygen delivery to the alveoli in COVID-19 is airway obstruction, an adequate screening model must necessarily include subtotal filling of the airway with viscous sputum.

Thus, to prevent irreversible damage to brain cells from hypoxia, it is necessary to immediately replace the viscous sputum in the alveoli of the lungs with oxygen gas. Therefore, the lungs should be the basis of the required screening model. Moreover, in the first stage, it is quite reasonable to use the isolated lungs of experimental animals for obtaining accelerated desired results. In this case, a standardized model suitable for biological screening can be obtained by using viable isolated lungs of a healthy experimental animal. To simulate respiratory obstruction, warm artificial sputum is used, which is injected through the trachea in a volume that provides subtotal filling of the airways of the lungs. For the purpose of standardization and safety of research, "Artificial sputum for modeling respiratory obstruction in COVID-19" was developed.[5]

The formulation of artificial sputum includes 4.4-22.0% potato starch, 2.2-11.0% gelatin, 0.9% sodium chloride, and 5% blood of an agricultural animal diluted with distilled water in a ratio of 1:1. Artificial sputum has a pH of 7.0-7.4, osmotic activity of 280-300 mosmol/L of water and a temperature of +37°C. Such artificial sputum has the "necessary" physicochemical and biochemical properties. In particular, such sputum has the "right" viscosity and contains the enzyme catalase.

This sputum provides urgent subtotal filling of the airways of isolated lungs of experimental animals. As a result, the lungs lose their airiness and drown in the water. It is these lungs that can be used as a biological model for screening expectorant, mucolytic, pyolitic, and antihypoxic drugs when inhaled or injected as intrapulmonary. Artificial sputum can be used for respiratory obstruction not only in isolated lungs, but also in the lungs of live healthy experimental animals. In this case, artificial sputum is injected in the same way through the trachea. The criterion of adequacy in live animals is a decrease in blood oxygenation. At the same time, the model of respiratory obstruction in live healthy experimental animals allows us to evaluate not only the effectiveness of airway recanalization, but also the effectiveness of blood reoxygenation.

In general, it seems that artificial sputum with traces of blood can be recommended for modeling airway obstruction in animals. This technique of respiratory obstruction can be used to assess the biological activity of pyolitic and antihypoxic drugs. It is the most appropriate approach to determine the strategy for the search and development of new drugs intended for urgent recanalization of the respiratory tract and reoxygenation of blood in patients with severe nonspecific pneumonia caused by COVID-19. The proposed model of airway obstruction can reduce the time and cost of screening, detection, and evaluation of the effectiveness of new drugs designed to urgently increase blood oxygenation in patients with severe hypoxia. It may well be that this search strategy will allow in the near future to develop drugs that can become a worthy alternative to ECMO and reduce the mortality of patients with COVID-19.

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Ethical statement
The study was approved by the Ethics Committee of the Institute of Thermology (№ 7 dated 27.09.2021, Izhevsk).

Competing interests
None to be declared.

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