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Information ProcCluster® SARS-CoV-2

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PROC-CLUSTER®

SARS-CoV-2

Inflamed pharma GmbH is a GMP-certified manufacturer of active ingredients, develops new applications for the active ingredient ProcCluster® and is continuously expanding the patent protection of ProcCluster®. The aim is to conduct clinical studies in the leading indications in order to establish ProcCluster® as a finished medicinal product and to enable broader areas of application for the active ingredient.
The GMP-compliant development of active ingredients and active ingredient precursors is the main field of activity of inflamed pharma GmbH. Inflamed has many years of experience in the formulation development of small molecules, which have unfavorable properties, such as poor water solubility or membrane permeability.

The GMP-compliant manufactured and patented active ingredient ProcCluster® (Procainium -hydrogen carbonate * sodium chloride) is a solid active ingredient based on the well-known active ingredient procaine. It has an almost physiological pH value (7.6), combines both hydrophobic and hydrophilic properties, is therefore water-soluble and penetrable and can not only act locally but also systemically. Procaine and consequently ProcCluster® belong to the group of local anesthetics (LA) of the ester type. ProcCluster® has been used since 2008 for the preparation of prescription drugs and since 2012 for the production of parenterals within the scope of permission-free in-house production according to §13 2b AMG.

Local anesthetics in general have multiple effects. In addition to the well-known anal-geological (via the blockade of the sodium channels) and anti-arrhythmic effects, this substance class has other effects, some of which are described as “alternative effects”. These include in particular anti-inflammatory, antithrombotic activity and vasodilation. The most frequently used alternative effects are the anti-inflammatory effects.

KEY BENEFITS

- Reduction of viral load >90%
- Reduction of cytokine release
- Enhancement of microcirculation
- GMP compliant manufacturing
- Established for different galenic forms

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Research activities around the world are in full swing to find drugs to treat COVID-19 diseases. It is already becoming apparent that there will be no such thing as “the one medication”, since the courses are very different, and the phase of the disease also plays an important role in the choice of drug treatment. In the early phase, the focus is on avoiding penetration (e.g. antiviral drugs) and reducing virus replication. In the second and third phase, the reduction of inflammation and thus the prevention of the cytokine storm (e.g. through immune modulators) is of greatest importance, as is medication for the treatment of pulmonary fibrosis or the prevention of blood clots. There are several drug or drug candidates that can be assigned to several of these categories, e.g. cancer drugs and drugs for the treatment of pancreatic inflammation or inflammatory bowel disease. ProcCluster® can also be classified in this group. It combines anti-inflammatory and vasodilatory effects. So far it is known that procaine influences the MAPK signal cascade, among other things. This in turn regulates, among other things, the expression of cytokines such as IL-6 but also the replication of many RNA viruses such as influenza, hanta, RS viruses (respiratory syntial virus) or SARS-CoV-2, which cause COVID-19. In cell culture experiments co-cultured with influenza and SARS-CoV-2, positive ProcCluster® effects regarding the reduction of the viral load have been demonstrated. https://biorxiv.org/cgi/content/short/2021.06.07.447335v1

It was shown that treatment with ProcCluster® leads to a concentration-dependent reduction in the viral mRNA synthesis of SARS-CoV-2 and influenza A viruses (IAV) of at least 90%. In the same way, the mRNA synthesis of various cytokines (IFNb, IL-6, IP-10) was reduced in the presence of ProcCluster® (PC) compared to untreated, infected cells.

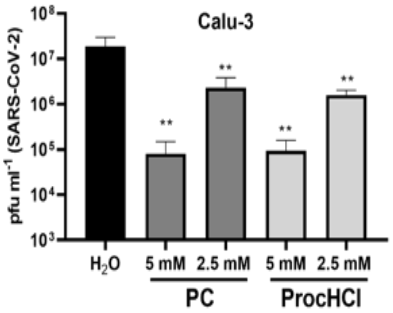

Fig. 1: ProcCluster® inhibits SARS-CoV-2 infection in vitro. Virus titers were examined using standard plaque assays.

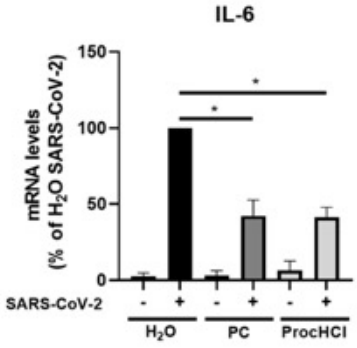

Fig. 2: ProcCluster® reduce the SARS-CoV-2 induced IL-6 production. The mRNA synthesis of SARS-CoV-2 (N1), cellular IL-6 was quantified using qRT-PCR.

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In order to visualize the extent of the SARS-CoV-2 infection and the IAV infection in the absence or presence of procaine, immunofluorescence microscopy examinations were carried out after 24 h p.i.. In untreated, SARS-CoV-2-infected samples, an accumulation of the spike protein is visible, which is reduced in ProcCluster®-treated samples. Accordingly, an accumulation of the IAV nucleoprotein (NP) is visible in the cytoplasm and in the cell nucleus of the infected cells, which indicates an ongoing replication, which is reduced in the presence of ProcCluster®.

These results indicate a ProcCluster®-mediated inhibition of viral infection. Since a characteristic of the serious illness of COVID-19, but also of the flu, is increased cytokine expression, which is associated with harmful inflammation and cell death, the influence of both substances on viral mRNA synthesis as well as SARS-CoV-2 and IAV-mediated cytokine and chemokine expression using qRT-PCR analysis after 24 h pi certainly.

Treatment with ProcCluster® leads to a reduced viral mRNA synthesis of SARS-CoV-2 and IAV.

An excessive inflammatory reaction also occurs in atypical pneumonia (also called interstitial pneumonia). This means that pathogens get into the interstitium, i.e. the tissue between the alveoli. The inflammatory process takes place in the framework of the lungs and not within the lungs. Therefore, membrane-permeable, non-acidic therapeutic agents such as ProcCluster® have a huge advantage, because they can reach easily the inflammation site.

An advantage of using substances that are not directed against the virus itself, but rather cellular factors that either inhibit virus replication or regulate harmful, excessive immune responses, is the reduced likelihood of the development of resistant virus variants. Since cellular targets of RNA viruses are also used for their own purposes at different times of the replication cycle, the attack by cellular factors not only offers the possibility of being used against SARS-CoV-2 or influenza virus infections.

In this way, the range of therapy is significantly expanded, and a wide range of use is made possible in the future.

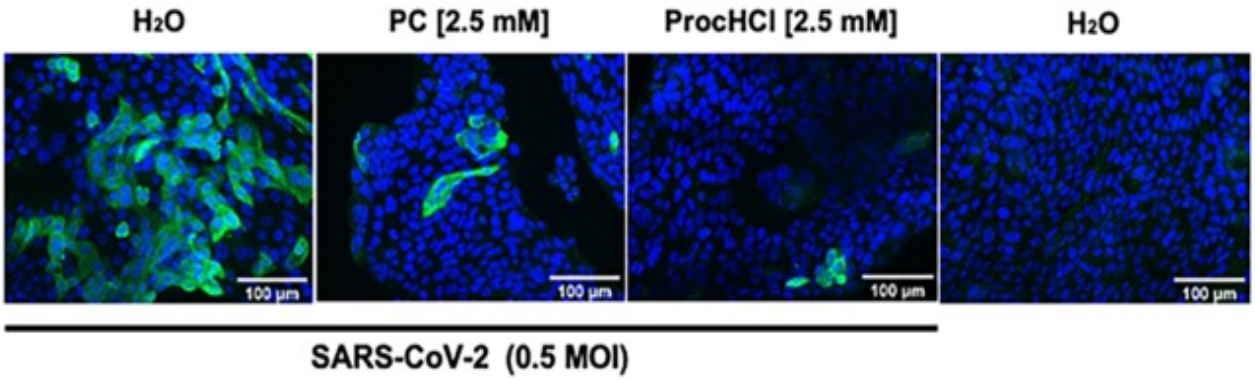

Fig. 3: Concentration-dependent SARS-CoV-2 reduction through ProcCluster®. Immunofluorescence microscopy shows the expression of the SARS-CoV-2 spike protein (green), cell nuclei were stained with Hoechst-33342 (blue).

FURTHER EFFECTS

Another effect that is often described and used in neural therapy, among others, is the influence on microcirculation. If the microcirculation is disturbed, the surrounding cells may not be adequately supplied with nutrients and oxygen and metabolic products may not be removed. The function and performance of the affected cells or organs is impaired. ProcCluster® improves the blood circulation and can especially positively influence the circulation in the very fine vessels and thus the functional state of the affected organ system.

Application observations of use with ProcCluster® on more than 50 patients with COVID infections, post-COVID syndrome or post-COVID vaccine reaction treated with capsules (prescription drugs) or parenterals (permission-free in-house production AMG §13 2b) showed a success of the treatment. Physical complaints such as chronic fatigue, exhaustion, persistent lack of energy, cognitive deficits (concentration, memory performance), pain in the limbs, joints and muscles, loss of smell and / or taste, dizziness, anxiety syndrome and shortness of breath were alleviated. Hospitalizations could be avoided.

Approving substances that are already used for other diseases is the most promising option for treating SARS-CoV-2 infections in the short term. New antiviral strategies target virus-supporting cellular factors that are used by viruses to support their own replication and spread. Further possibilities exist in the inhibition of excessive immune reactions or in the active dissolution of inflammatory processes.

One possible therapeutic approach is ProcCluster®, which, in addition to inhibiting excessive immune reactions or actively dissolving inflammatory processes, can also reduce the viral load and positively influence the microcirculation. (ProcCluster® patents: PCT / EP2018 / 074089; priority registration in Europe No. EP 21157974.3)

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