Inhibition of the binding of the spike protein of COVID-19 virus to lung cells by ectoine

SARS-Coronavirus 2 (SARS-CoV-2) has rapidly become a global challenge and has led to a worldwide pandemic. Currently, there is no targeted treatment of COVID-19 diseases caused by SARS-CoV-2. Against this background, medical devices and drugs with preventive effects are of particular importance. Ectoin®-based medical products from bitop have been used successfully for years. A current *in-vitro* study by bitop shows the preventive effect of ectoine also for COVID-19 resp. SARS-CoV-2 infections. The spike protein (S-protein) of SARS-CoV-2 plays a central role in viral infection and pathogenesis of COVID-19. S-protein recognizes and locks onto ACE2 host receptor of lung and other human cells and facilitates the fusion between the virus envelope and the host cell membrane. This is the initial step of cellular infection (Fig. 1) by SARS-CoV-2 (COVID-19).

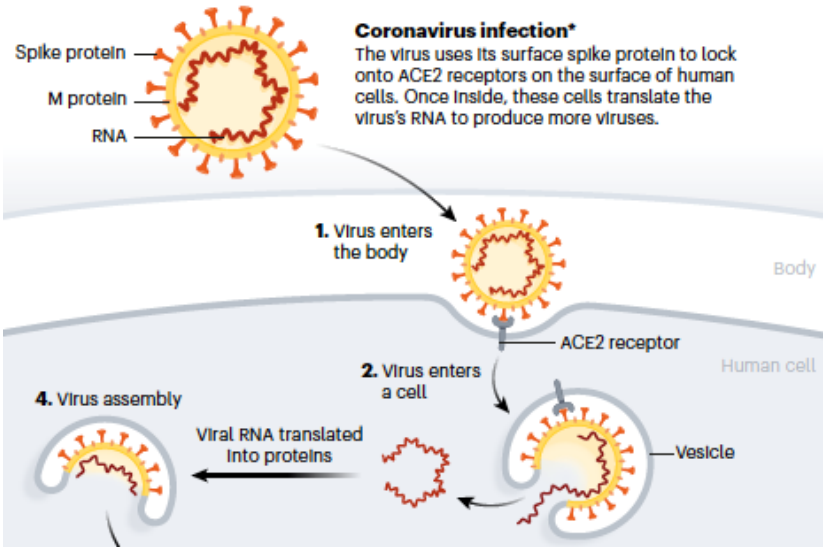

Fig. 1: Initial step of COVID-19 infection (from "The race for corona virus vaccines"; Ewen Callaway; Nature Vol. 580, 30 April 2020)

bitop developed a new *in-vitro* assay to investigate the binding efficacy of S-protein to A549 lung cells (presenting the ACE2 receptor) at different concentrations of ectoine and S-protein. For the experiment the cells were pre-treated with different concentrations of ectoine and different concentrations of recombinant produced SARS-CoV-2 Spike protein. The binding of S-protein is analyzed by indirect immunofluorescence. The cells are incubated after washing with a murine antibody directed against the HIS tag of the S-protein. After washing the cells are incubated with an alexafluor 488 labeled secondary antibody. The fluorescence of the cells is then analyzed by flow cytometry. The aim of this in-vitro study was to test the influence of the substances ectoine and γ-NADA (precursor of ectoine as a control substance) on binding of the spike-protein SARS Cov2 S to A549 lung cells presenting the ACE2 receptor. The results show that ectoine inhibits efficiently the binding of the protein to A549 cells at all tested concentrations. The optimal concentration range is between 1,25% - 5% ectoine (Fig. 2).

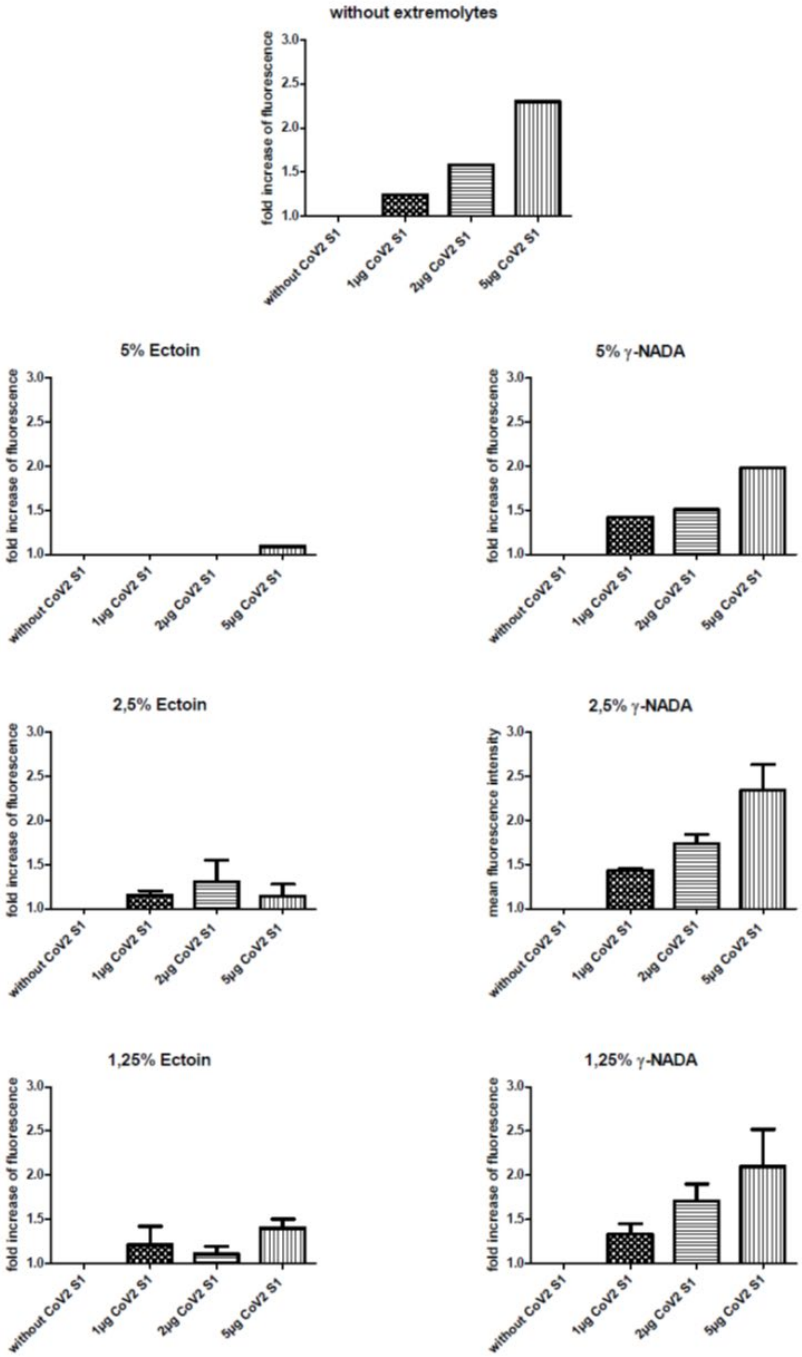

Fig. 2: Increase of fluorescence of A549 cells due to the binding of the CoV2 S-protein to the cell surface. Ectoine already shows a positive effect at 1.25% and inhibits the binding of the CoV2 S-protein to A549 cells. For NADA as a control no significant effect can be observed**.**

The effect of the suppression of S-protein binding to the ACE2 receptor is explained by the protein and membrane stabilizing effect of ectoine. Ectoine accumulates around the respective binding partners, here in particular around the peplomers of the spike protein and shields them via a hydrate envelope. The conformation of the folded protein is stabilized and thus the accessibility of the receptor-binding domain is reduced. Therefore, ectoine as a highly tolerable active ingredient in medical products has a great potential for prevention of COVID-19 diseases.