Author Correction: In vitro virucidal activity of Echinaforce®, an Echinacea purpurea preparation, against coronaviruses, including common cold coronavirus 229E and SARS-CoV-2

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Following publication of the original article [1], the authors would like to make some clarifications:

Clarification
In the publication "In vitro virucidal activity of Echinaforce®, an Echinacea purpurea preparation, against coronaviruses, including common cold coronavirus 229E and SARS-CoV-2", we describe the virucidal activity of a commercially available formulation, Echinaforce®, against coronaviruses. Our aim was to evaluate the antiviral activity of the product as a whole, rather than specifically investigating the properties of individual components. To this end, we diluted Echinaforce® in cell culture media, 320 times (50 µg/mL) and 1600 times (10 µg/mL). Since our goal was to evaluate the whole extract, we assessed the appropriate negative control as cell culture media alone, rather than the ethanol extraction media used for the Echinacea extraction and production of the product. The concentration of ethanol in the Echinaforce® extract is 65%. However, in our final treatment dilutions, residual ethanol concentrations are 0.2% and 0.04% for 50 µg/mL and 10 µg/mL, respectively. Inactivation of SARS-CoV-2 and other coronaviruses with alcohol-based disinfectants has been shown to require higher concentrations (≥30% v/v) (1, reviewed in 2).

Therefore, in our discussion, we hypothesize that this observed virucidal effect could be due to Echinacea as it has been shown to affect the infectivity of other viruses, when dissolved in either water or ethanol (3). The authors would like to emphasize that direct contact with virus particles is required for virucidal activity and due to the oral administration of Echinaforce® it is currently unclear how relevant this is for in-vivo situations. Data on the potential benefits of regular intake of Echinacea for respiratory tract infections is available (4, 5, 6, reviewed in 7) but further research is needed. The authors would like to emphasize that any hypotheses made about the effectiveness of Echinaforce® against SARS-CoV-2 in-vivo are theoretical and would need to be investigated in clinical studies (reviewed in 8).
In the current study, we state that the product Echinaforce® - as is – exhibits virucidal activity against four coronaviruses *in-vitro*, upon direct contact in suspension.

Due to concerns regarding the residual ethanol concentrations in our treatment dilutions, we have provided additional data showing no statistical difference in virus replication of viruses previously shown to be sensitive to Echinaforce® between cell culture media and media containing the residual ethanol concentration in our highest treatment dilution (0.2% - “Media + EtOH”) (Fig. 1).

**Methods**

**Echinaforce® treatment**

1 × 10⁴ TCID₅₀/ml HCoV-229E and 1 × 10⁵ PFU/ml MERS-CoV, SARS-CoV-1 and -2 and YFV were incubated with Echinaforce diluted to 50 µg/ml in 2%-FBS-DMEM (HCoV-229E) or 2%-FBS-MEM and incubated for 1 h at room temperature (RT) on a rocking platform. Cell culture media alone and media containing the corresponding residual ethanol concentration (0.2%) was incubated in the same way.

**Limiting dilution assay (TCID₅₀)**

Residual infectivity of HCoV-229E, SARS-CoV-1 and -2, MERS-CoV and YFV was determined by a limiting dilution assay (TCID₅₀) on Huh7 (HCoV-229E), Vero (YFV) or Vero E6 (SARS-CoV-1 and -2, MERS-CoV) cells according to the Spearman-Kärber algorithm as described by Hierholzer and Killington (1996).

**Statistical analysis**

To determine statistical significance, Kruskal-Wallis non-parametric test with Dunn’s multiple comparisons test was applied to all data sets using GraphPad Prism.
version 7.05. P-values < 0.05 were considered statistically significant.

Conflict of interests:
W.C. Albrich wishes to clarify his conflict of interest statement as follows:
While W. C. Albrich has been the recipient of fees and research grants from A. Vogel AG that were paid to his institution, no fees or research grants were received in relation to this article.

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Due to a typesetting misunderstanding, some cells were merged in the Table 3. The following table displays information correctly. No data have changed from the version originally published.

Table 3 Overview of viruses used in the current study

| Name                      | Strain        | Propagated in | Medium*                                          | Procured from                                      |
|---------------------------|---------------|---------------|--------------------------------------------------|----------------------------------------------------|
| HCoV                      | 229E          | Huh-7, 33 °C  | DMEM +5%FBS, 2 mM Glutamine, non-essential amino acids, Pen/strep, HEPES (Biochrom, Germany) | Prof. Volker Thiel, University of Bern, Switzerland (24, 25) |
| MERS-CoV                   | EMC           | Vero, 37 °C   | DMEM +2%FBS, 2 mM Glutamine, non-essential amino acids, Pen/strep, HEPES (Biochrom, Germany) | Prof. Volker Thiel, University of Bern, Switzerland (24, 25) |
| SARS-CoV                   | Frankfurt-1   | Vero, 37 °C   | DMEM +2%FBS, 2 mM Glutamine, non-essential amino acids, Pen/strep, HEPES (Biochrom, Germany) | Prof. Volker Thiel, University of Bern, Switzerland (24, 25) |
| SARS-CoV-2                 | BetaCoV/France/IDF0372/2020 | Vero E6, 37 °C | DMEM +2%FBS, 2 mM Glutamine, non-essential amino acids, Pen/strep, HEPES (Biochrom, Germany) | Institute Pasteur, Paris, France via EVAg, European Virus Archive |
| Mouse parvovirus           | MVM Prototype, ATCC-1346 | A9, 37 °C | DMEM +2%FBS, 2 mM Glutamine, non-essential amino acids, Pen/strep, HEPES (Biochrom, Germany) | The National Collection of Patho-genic Viruses, UK |
| Yellow Fever virus         | 17D, NCPV-0507 | Vero, 37 °C   | DMEM +2%FBS, 2 mM Glutamine, non-essential amino acids, Pen/strep, HEPES (Biochrom, Germany) | The National Collection of Patho-genic Viruses, UK |
| Vaccinia virus             | Elstree (Lister Vaccine), ATCC-VR-1549 | Vero, 37 °C | DMEM +2%FBS, 2 mM Glutamine, non-essential amino acids, Pen/strep, HEPES (Biochrom, Germany) | The National Collection of Patho-genic Viruses, UK |
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