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# Caffeic Acid

Domina Petric, MD

**ABSTRACT:** Caffeic acid is one of the pharmacologically active compounds of many medicinal herbs including *Echinacea purpurea* which was recently recommended as prophylactic treatment for all coronaviruses, including newly occurring strains, such as SARS-CoV-2. Cell-surface heparan sulfate proteoglycans (HSPGs) provide the binding sites for SARS-CoV invasion at the early attachment phase. In addition to ACE2, HSPGs are essential cell-surface molecules involved in SARS-CoV cell entry. Caffeic acid might be a potent molecule for the treatment of new SARS-CoV-2 virus.

**Caffeic acid** is one of the pharmacologically active compounds of many medicinal herbs including *Echinacea purpurea* which was recently recommended as prophylactic treatment for all CoVs, including newly occurring strains, such as SARS-CoV-2<sup>1</sup>.

Organic compounds with a **caffeoyl moiety** (caffeic acid, rosmarinic acid, chicoric acid, etc.) have antiviral properties towards herpes simplex (HSV), influenza and immunodeficiency viruses (HIV).

The study conducted by Langland and coworkers (2018) evaluated the HSV antiviral properties of caffeic acid when paired with a variety of metal and other inorganic ions. The results demonstrated that the antiviral activity of caffeic acid increased upwards of 100-fold by the addition of cations, such as  $\text{Fe}^{3+}$ , and

anionic molecules, such as molybdate and phosphate. Cellular toxicity tests of the caffeic acid chelates showed that they have low toxicities with selectivity indices ( $\text{TD}_{50}/\text{EC}_{50}$ ) for  $\text{Fe}^{3+}$ ,  $\text{MoO}_4^{2-}$ , and  $\text{PO}_4^{3-}$  chelates being 1700, >540, and >30. Caffeic acid paired with  $\text{Fe}^{3+}$  was tested against eight strains of viruses, including those from different families. The caffeic acid chelates were mostly effective against HSV1 and HSV2, but they also had moderate activity against vaccinia virus and a VSV-Ebola pseudotyped virus. All the viruses that were strongly impacted by the caffeic chelates require **heparan sulfate proteoglycans** for cellular attachment, so it is likely that caffeic chelates target and interfere with this mechanism. Since the caffeic acid chelates target an extra-cellular process, they might be able to be combined with existing

medications, such as acyclovir, that target an intracellular process to achieve greater viral control<sup>2</sup>.

Cell-surface heparan sulfate proteoglycans (HSPGs) provide the binding sites for SARS-CoV invasion at the early attachment phase. In addition to ACE2, HSPGs are essential cell-surface molecules involved in SARS-CoV cell entry<sup>3</sup>.

In the study (Weng et al, 2019) *Sambucus FormosanaNakai* extract reduced cytopathicity and virus yield in human coronavirus NL63, HCoV-NL63-infected cells. Among phenolic acid constituents, **caffeic acid**, chlorogenic acid and gallic acid sustained the anti-HCoV-NL63 activity. *Sambucus FormosanaNakai* extract and caffeic acid concentration-dependently inhibited HCoV-NL63 attachment onto cells<sup>4</sup>.

## CONCLUSION

Cell-surface heparan sulfate proteoglycans (HSPGs) provide the binding sites for SARS-CoV invasion at the early attachment phase. In addition to ACE2, HSPGs are essential cell-surface molecules involved in SARS-CoV cell entry.

All the viruses investigated in previous studies that were strongly impacted by the caffeic acid chelates require heparan sulfate proteoglycans for cellular attachment.

Caffeic acid is one of the pharmacologically active compounds of many medicinal herbs including *Echinacea purpurea* which was recently recommended as prophylactic treatment for all CoVs, including newly occurring strains, such as SARS-CoV-2.

Therefore, caffeic acid might be a potent molecule for the treatment of new SARS-CoV-2 virus, especially if pared with  $\text{Fe}^{3+}$  ions (caffeic acid  $\text{Fe}^{3+}$  chelate) or other ions ( $\text{MoO}_4^{2-}$  and  $\text{PO}_4^{3-}$  chelates).

## REFERENCES

1. Signer J, Jonsdottir HR, Albrich WC, et al. In vitro antiviral activity of Echinaforce®, an *Echinacea purpurea* preparation, against common cold coronavirus 229E and highly pathogenic MERS-CoV and SARS-CoV. *Virology*. 2020. DOI: 10.21203/rs.2.24724/v1
2. Langland J, Jacobs B, Wagner CE, Ruiz G, Cahill TM. Antiviral activity of metal chelates of caffeic acid and similar compounds towards herpes simplex, VSV-Ebola pseudotyped and vaccinia viruses. *Antiviral Res*. 2018;160:143-150.
3. Lang J, Yang N, Deng J, et al. Inhibition of SARS pseudovirus cell entry by lactoferrin binding to heparan sulfate proteoglycans. *PLoS One*. 2011;6(8):e23710.
4. Weng JR, Lin CS, Lai HC, et al. Antiviral activity of *Sambucus Formosana* Nakai ethanol extract and related phenolic acid constituents against human coronavirus NL63. *Virus Research*. 2019;273:197767.