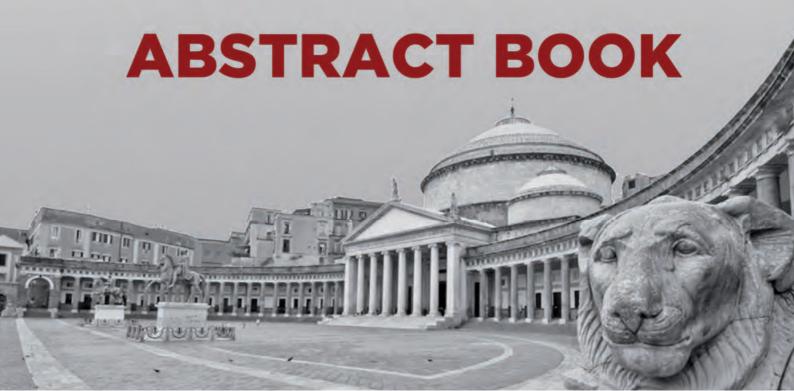


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IN VITRO ANTIVIRAL ACTIVITY OF A CRANBERRY VACCINIUM MACROCARPON EXTRACT AGAINST EBOLA VIRUS AND RABIES VIRUS

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Emerging and reemerging viral infections represent a major concern for human and veterinary public health and there is an urgent need for the development of broad-spectrum antivirals.

We have recently observed that a cranberry (*Vaccinium macrocarpon*) extract, which contains high levels of A2-type proanthocyanidins (PAC-A2), inhibits influenza A and B viruses [1], herpes simplex virus type 1 and 2 [2], and Crimean-Congo Hemorrhagic Fever Virus [3] *in vitro* replication by interfering with the adhesion/internalization stage of the viral life cycle. In this work, we have evaluated the antiviral activity of the cranberry extract against two highly pathogenic viruses, such as Ebola Virus (EBOV) and Rabies Virus (RABV).

To evaluate the antiviral activity of the cranberry extract, a recombinant Vesicular Stomatitis Virus (pVSV) vector expressing the luciferase reporter was adopted. The pVSV was pseudotyped either with the EBOV or RABV glycoproteins. Time-of-addition, viral attachment, and entry assays were performed on Vero CCL-81 in the presence of different concentrations of the cranberry extract. Finally, experiments with infectious EBOV and RABV were performed to validate the results obtained with pseudovirus.

The cranberry extract showed an inhibitory activity against both the pVSV-EBOV and pVSV-RABV infection. Treating target cells or the pseudovirus with the compound before or during the infection phase determined a significant reduction of viral infectivity. In contrast, only a modest inhibition was detected when cells were treated with the extract after virus internalization. The antiviral activity of the cranberry extract was confirmed against the live EBOV, while experiments are ongoing for RABV.

In Conclusions:

- The cranberry extract inhibits EBOV and RABV infection acting at the early stages of their replicative cycles.
- This broad-spectrum antiviral activity suggests this cranberry extract (or its components) as a promising antiviral candidate against emerging and re-emerging viral infections.

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