Several viruses of great importance in public health are included in the Flavivirus genus, such as Dengue virus (DENV), Saint Louis Encephalitis virus (SLEV), Yellow fever virus (YFV), and Zika virus (ZKV). SLEV is widely distributed in the Americas and can cause diverse clinical signs varying from febrile syndromes to fatal meningoencephalitis. Similarly to other viruses, there is still no effective treatment against SLEV. A new approach for treatment lies in the search for cellular proteins as therapeutic targets, since the viruses as obligatory intracellular parasites, use various components of the cellular machinery for their replication. Previous studies, demonstrated that pharmacological inhibitors of cellular protein kinases exhibit a potential antiviral activity against different Flaviviruses, including pharmacological inhibitors of members of Src/Abl (saracatinib and bosutinib) and MEK/ERK (U0126 and selumetinib) protein kinase families. Given the similarity in the multiplication cycles among members of this genus, the current work intends to investigate the potential antiviral effect resulting from the association of these pharmacological inhibitors, which can act at different steps of the SLEV multiplication cycle and its effect on virus multiplication in vitro. For this end, different combinations of inhibitors were tested aiming to find the minimum concentrations (MC) capable of promoting the reduction of at least one logarithmic unit in the viral titer. A Western blot assay was performed, where the MCs able to inhibit the phosphorylation of the respective kinases were determined and, subsequently, the MCs to be tested were chosen. Next, dose-response assays were performed to determine the combinations that showed a possible antiviral effect. No significant reduction in viral titer was observed in all combinations tested between selumetinib and bosutinib inhibitors. However, when (selumetinib) was replaced with other MEK/ERK inhibitor (refametinib), the reduction was more expressive when compared to the individual antiviral action of both inhibitors. Drug association studies are widely used and aim to minimize side effects, by decreasing doses used and, consequently, reducing a potential drug resistance.

Keywords: Saint Louis Encephalitis virus, Src, MEK/ERK, Virus-host interaction, Antiviral.