

## Phenolic Acids of Plant Origin as Promising Compounds for Elaboration of Antiviral Drugs against Influenza

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**Abstract :** Introduction: Influenza viruses could infect approximately 5% to 10% of the global human population annually, resulting in serious social and economic damage. Vaccination and etiotropic antiviral drugs are used for the prevention and treatment of influenza. Vaccination is important; however, antiviral drugs represent the second line of defense against new emerging influenza virus strains for which vaccines may be unsuccessful. However, the significant drawback of commercial synthetic anti-flu drugs is the appearance of drug-resistant influenza virus strains. Therefore, the search and development of new anti-flu drugs efficient against drug-resistant strains is an important medical problem for today. The aim of this work was a study of four phenolic acids of plant origin (Gallic, Syringic, Vanillic, and Protocatechuic acids) as a possible tool for treatment against influenza virus. Methods: Phenolic acids; gallic, syringic, vanillic, and protocatechuic have been prepared by extraction from plant tissues and purified using high-performance liquid chromatography fractionation. Avian influenza virus, strain A/Tern/South Africa/1/1961 (H5N3) and human epidemic influenza virus, strain A/Almaty/8/98 (H3N2) resistant to commercial anti-flu drugs (Rimantadine, Oseltamivir) were used for testing antiviral activity. Viruses were grown in the allantoic cavity of 10 days old chicken embryos. The chemotherapeutic index (CTI), determined as the ratio of an average toxic concentration of the tested compound ( $TC_{50}$ ) to the average effective virus-inhibition concentration ( $EC_{50}$ ), has been used as a criteria of specific antiviral action. Results: The results of study have shown that the structure of phenolic acids significantly affected their ability to suppress the reproduction of tested influenza virus strains. The highest antiviral activity among tested phenolic acids was detected for gallic acid, which contains three hydroxyl groups in the molecule at C3, C4, and C5 positions. Antiviral activity of gallic acid against A/H5N3 and A/H3N2 influenza virus strains was higher than antiviral activity of Oseltamivir and Rimantadine. gallic acid inhibited almost 100% of the infection activity of both tested viruses. Protocatechuic acid, which possesses 2 hydroxyl groups (C3 and C4) have shown weaker antiviral activity in comparison with gallic acid and inhibited less than 10% of virus infection activity. Syringic acid, which contains two hydroxyl groups (C3 and C5), was able to suppress up to 12% of infection activity. Substitution of two hydroxyl groups by methoxy groups resulted in the complete loss of antiviral activity. Vanillic acid, which is different from protocatechuic acid by replacing of C3 hydroxyl group to methoxy group, was able to suppress about 30% of infection activity of tested influenza viruses. Conclusion: For pronounced antiviral activity, the molecular of phenolic acid must have at least two hydroxyl groups. Replacement of hydroxyl groups to methoxy group leads to a reduction of antiviral properties. Gallic acid demonstrated high antiviral activity against influenza viruses, including Rimantadine and Oseltamivir resistant strains, and could be used as a potential candidate for the development of antiviral drug against influenza virus.

**Keywords :** antiviral activity, influenza virus, drug resistance, phenolic acids

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