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Fruit peels as a vehicle for the availability of phenolic compounds with anti-influenza virus activity

Gilberto Mercado Mercado, Delia Libier Hernández de la Rosa

Resumen

Influenza is a virus that infects the respiratory tract causing high mortality rates. There are about 100 strains of this virus, the most frequent being Rhinovirus and Coronavirus. Fruit peels are studied due to the amount of phenolic compounds (PC) with multiple positive health functions. There is evidence that PCs have great antiviral potential. The efficacy of the antiviral activity depends on the hydroxylation, methoxylation and alkylation of several components of the PC ring. Quercetin, gallic acid, epigallocatechin, catechin are some PCs that have been proven to have activity against influenza virus by blocking entry into host cells. Haloflavanes are synthetic flavonoids that have become of interest for their pharmacological properties as antiviral agents. These compounds aim to obtain improvements on those of natural, non-fluorinated flavonoids. The wide variety of mechanisms of action of PCs against viral infections could be applied as a natural pharmaceutical treatment strategy. The present review highlights the importance of fruit peels as a PC-enriched material with potential antiviral properties against influenza virus.

Keywords:

antiviral activity; influenza virus; common cold; peel; phenolic compounds.

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Introduction

Influenza is an emerging acute respiratory disease that can be spread from person to person through droplets that remain suspended in the air after a person with influenza coughs or sneezes. Influenza viruses belong to the *Orthomyxoviridae* family; they pass through the respiratory tract, complicating the health of people regardless of age; however, children, young people and the elderly are more vulnerable, especially during the winter season. For this reason, people resort to self-medication causing the virus to become resistant to antibiotics, increasing the contagion and spreading in the nose, throat, bronchial tubes and lungs, which can last approximately 14 days.

People infected with influenza also resort to rest, consumption of fruit juices or other liquids, home remedies, gargling with warm salt water, cough drops and medications to relieve body pain, but the disease may recur more frequently and even cause the appearance of other conditions (i.e. pneumonia) or even death. In this regard, alternatives are sought to mitigate the disease with alternative components that have the potential to reduce the ailment (Zhu et al., 2023). Fruit peels are an emerging resource that have been shown to contain antiviral compounds, such as phenolic compounds (PC), which various studies have shown can act by inhibiting the activity of viruses such as SARS-CoV-2, inovirus, adenovirus, coronavirus, metapneumovirus, and influenza (Ninfali et al., 2020). Therefore, this chapter aims at describing the pharmaceutical value of PCs present in fruit peels and their antiviral properties.

Influenza characteristics

Influenza, colloquially called flu, is an infection that is easily transmitted from person to person through respiratory secretions with the appearance of nasal congestion, sneezing, fluid, watery and abundant rhinorrhea, discomfort and itching in the throat, dry cough, muscle aches, headache, bronchial and, occasionally, in the lungs; having an approximate duration of 10 to 13 days with temperature ranging between 38 to 41°C (Krammer et al., 2018). This disease is transmitted by inhaling particles (<5 μm in diameter) suspended in the air affecting people at any age group, mainly children <2 years, elderly >65 years, pregnant women and patients with pathologies (chronic diseases, diabetes, neuropathies, cystic fibrosis, asthma, neoplastic diseases), so it has become a serious problem due to high morbidity and mortality. Nowadays, it is common to confuse between common cold and flu; although they share some symptoms, it is common to make the mistake of mentioning these pathologies indistinctly, so it is important to highlight the differences as described in Table 1 (Shie and Fang, 2019; Krammer et al., 2018).

Table 1. Differences in symptoms between the common cold and the influenza (Czubak et al., 2021).

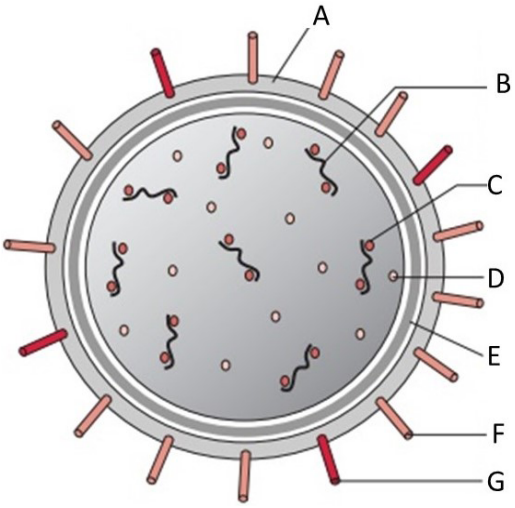
Symptomatology	Common cold	Influenza
Incubation time (h)	48–72	18–36
Aches and pain	Slight	Assiduous, usually severe
Onset	1-2 days	Rapid
Fever	Rare	Common
Chills	Rare	Sometimes
Sneezing	Common	Rare
Stuffy/Runny nose	Common	Sometimes
Headache	Sometimes–sinus	Sometimes
Cough	Common	Common
Myalgia	Sometimes	Assiduous
Low back pain	Assiduous	Assiduous
Odynophagia	Assiduous	Sometimes
Eye irritation	Assiduous	Sometimes
Fatigue or weakness	Sometimes	Usually lasting up to 3 weeks
Extreme exhaustion	Never	Within the first few days and Frequent
Chest discomfort	Moderate	Assiduous

Source: authors

Morphology and organization of the genome and coding proteins of the influenza virus

Influenza is found within the *Orthomyxoviridae* family, which refers to the affinity it has for mucin, a mucoprotein present in the mucus of various secretions, epithelial receptors, red blood cell membrane and serum. The virus is grouped into A, B, C, Thogovirus and Isavirus (Table 2), being genus A the most common and leading with higher infection and incidence of morbi-mortality in humans due to the capacity of mutation and constant evolution, which leads to make resistant to antigenic (Zhu et al., 2023). Influenza viruses of genus A, B, and C have a variable appearance (spherical or filamentous) with an average diameter of 100 nm and 300 nm in length (Figure 1), while the structure of genus C is usually in the form of a cord of about 500 nm (Krammer et al., 2018).

Figure 1. Morphological structure and components of the influenza virus.



Note: A) Lipid membrane of envelope; B) Segments of single-stranded RNA; C) Nucleoprotein; D) Polymerase; E) Matrix protein; F) hemagglutinin; G) neuraminidase.

Table 2. Taxonomy and genetics characteristics of influenza virus.

Generes	kingdom	Phylum	Class	Order	Family	serotypes or lineages	Morphology	Virion structure	D (nm)	RNA	Pathway of entry
Type α-	Orthornavirae	Negarnaviricota	Insthoviricetes	Articulavirales	Orthomyxoviridae	18 serotypes	Nucleocapsid surrounded by HA- and NA-antigen-coated envelope	Spherical or filamentous	80 -100	8 segments	Mucous
Type β						2 linages: B/ Yamagata y B/Victoria		Spherical or filamentous	80 -130	8 linear, single-chain, negative polarity segments	
Type γ						unique		Spherical or filamentous		single-stranded, segmented and with negative polarity	
Thogoto virus						3 serotypes: THOV BATV DHOV	Enveloped nucleocapsid	Spherical		6 segmentos en el THOV 7 segments in DHOV	
Isavirus	Riboviria					unique		Usually rounded and filamentous	90–120	8 segments	

D: diameter; ISA: salmon infection causing anemia; THOV: Thogoto virus; BATV: Batken virus; DHOV: Dhori virus; HA: hemagglutinin; NA: neuraminidase.

The influenza virus has a lipid envelope in which hemagglutinin (HA), neuraminidase (NA) and small amounts of M2 protein are embedded. Inside is the matrix protein, which surrounds the viral genome, coated by proteins (PB1, PB2 and PA) that make up the RNA polymerase and the NP nucleoprotein. The viral genome comprises 13,588 nucleotides that are fragmented by The viral genome comprises 13,588 nucleotides, which is fragmented by eight single-stranded RNA segments of different sizes (890 to 2,350 nucleotides) and encodes eleven viral proteins. The genome can undergo variations in the type of H and N proteins, t his causes RNA segments to be exchanged between two or more different viruses in the same cell, giving rise to new variants (Medina and García-Sastre, 2011). For this reason, there are currently >120 virus strains, the most frequent being Rhinovirus which prevails in autumn and spring and Coronavirus in late autumn and winter (Zhu et al., 2023).

The glycoprotein HA is found to express approximately 80% of viral surface glycoproteins forming homotrimers of cylindrical shape. Each homotrimer is confirmed by a fibrous stalk, which at one end inserts into the viral membrane, while at the other end is the globular domain with three binding sites for sialic acid. Thus, sialic acid defines the particular tropism of influenza viruses due to the specificity that different virus strains have for different types of sialic acid bonds with the preceding galactose in the carbohydrate chain. Thus, HA binds to sialic acid residues attached to galactose via 2,6-galactoside linkages. Epithelial cells lining the human trachea have mainly α2,6-linked carbohydrates (Noda, 2011). The HA1 subunit is responsible for binding to sialic acid-containing receptors, which affinity determines their pathogenicity in human cells. The HA2 subunit participates in the fusion between the viral membrane and the endosomal membrane. The endosome containing the virion is acidified causing a conformational change in HA2 that allows the strangulation of the viral and endosomal membranes, releasing the ribonucleoprotein into the cytoplasm (Jones et al., 2020; Noda, 2011).

On the other hand, NA has the function of cleaving the bonds between HA and sialic acid in order to release the virion from the infected cell. NA is found on the surface of the virion forming a homotetramer, each monomer is composed of a cytoplasmic domain, a transmembrane region, a hypervariable stalk, and a globular head that has the catalytic domain of this enzyme, with highly conserved regions in its active site. Other functions of NA include preventing the aggregation of released virions and breaking the N-acetyl-neuraminic acid bonds of the mucus so that the virus can establish itself in the upper respiratory tract (Krammer et al., 2018).

Once the virus has bound to its receptor in the cell, it enters the cytoplasm by endocytosis and the low pH of the endosome causes a change in the conformation of the virus hemagglutinin protein, which favors the fusion of the cell and viral membranes,

allowing the viral particle to enter the cytoplasm of the cell. The acidic pH within the endosome favors the dissociation of the ribonucleoproteins associated with the viral genome. The M2 protein allows the entry of protons into the viral particle and releases the viral genome, which enters the cell nucleus and initiates its transcription and replication. The viral messenger RNA is translated to form the corresponding proteins, and finally the new viruses assemble in the cell cytoplasm and exit by budding through the plasma membrane, which has been previously modified by the insertion of the viral proteins HA, NA and M2 (Kausar et al., 2021).

Antiviral treatment

The drugs focus on inhibiting NA activity and stopping viral shedding and disease development. Drug treatment for influenza virus has been shown to reduce the severity and days of symptoms. There are two classes of antivirals for the treatment of influenza, adamantanes and NA inhibitors (Table 3). The adamantanes block the M2 protein ion channel so that they inhibit the intracellular release of the virus; while the viral NA inhibitors prevent the release of viruses into the respiratory tract and their subsequent dissemination (Swierczynska et al., 2022; Kausar et al., 2021).

Table 3. Specifications of commercial drug classes for adamantanes and neuraminidase inhibitors.

Antiviral drugs	Presentation	Dosage (mg/Kg)	Bioactivity	Side effects
		Adamantians		
Amantadine	Capsule, tablet, liquid	100 – 200	Acts on viral particle attachment and DNA release and prevents virus fusion with the vacuolar membrane	Lymphatic system: leukopenia, reversible increase in liver enzymes Nervous system: somnolence or insomnia, depression, agitated states, vertigo, headaches, hallucinations, confusion, dizziness, lethargy, nightmares, ataxia, slurred speech, convulsions, disorientation, psychosis, tremor, dyskinesia, neuroleptic syndrome Cardiac system: leg edema, livedo reticularis, orthostatic hypotension, palpitations, congestive heart failure, heart failure Gastrointestinal system: dry mouth, nausea, anorexia, vomiting and constipation, diarrhea Skin and subcutaneous tissue disorders: diaphoresis, skin rashes, photosensitivity Ocular system: blurred vision, corneal lesion (punctate subepithelial opacities associated with superficial punctate keratitis, corneal epithelial edema and markedly decreased visual acuity) Musculoskeletal and connective tissue disorders: myalgia Renal and urinary disorders: urinary retention, urinary incontinence Impulse control: compulsive gambling, increased libido, hypersexuality
Rimantadine (Gabirol®)	Capsules or oral suspension	5 - 150 (kids)	Inhibits influenza A virus replication by altering the release of viral RNA into the host cell, interfering with the transmembrane function of the M2 viral protein ion channel	Nervous system: insomnia, dizziness, headache, "nervousness", fatigue, difficulty concentrating and sleeping Digestive system: nausea, vomiting, anorexia, dry mouth, abdominal pain Asthenia, hypersensitivity
		Neuraminidase inhibitors		
Oseltamivir (Tamiflu®)	Capsules or oral suspension	30 mg/10 – 15 Kg 45 mg/15 – 23 Kg/d 60 mg/23 – 40 Kg/d 75 mg/>40 Kg/d	It selectively inhibits NA, responsible for releasing the virus from infected cells and favoring its dissemination, therefore, the drug interferes in the stages of aggregation and release of viral particles	Lymphatic system: liver function disorders and jaundice Nervous system: headaches, hallucinations, delirium, nightmares, ataxia, anxiety, convulsions, neuropsychiatric disorders Cardiac system: low blood pressure and shortness of breath, seizure, heart rhythm disturbances, fatigue Gastrointestinal system: nausea, vomiting and gastrointestinal bleeding Skin and subcutaneous tissue disorders: peeling of the skin, blistering, allergic reactions with swelling of the face, skin, neck, including eyes and tongue, itchy rash, skin rashes Ocular system: conjuntivitis Musculoskeletal and connective tissue disorders: pain in the extremities, Stevens-Johnson syndrome and epidermal necrolysis Hearing system: inflammation of the ears and tympanic membrane disorder Nasopharyngeal system: sore throat, cough, bronchitis
Zanamivir (Relenza®)	Vials	10 (adults and seniors)	Inhibidor de la neuraminidasa	Lymphatic system: risk of anaphylactic reactions, hepatocellular lesion, increased of ALT y/o AST Respiratory system: bronchospasm and/or decreased respiratory function Nervous system: dizziness, delirium, hallucinations, hallucinations Gastrointestinal system: diarrhea Skin and subcutaneous tissue disorders: erythema multiforme, toxic epidermal necrolysis, Stevens-Johnson syndrome

Antiviral drugs	Presentation	Dosage (mg/Kg)	Bioactivity	Side effects
Peramivir	Vials	12 (2 – 17 years) 600 (adults)	ND	Lymphatic system: itching/swelling (face/tongue/throat), wheezing, hoarseness Nervous system: confusion and hallucinations, nervousness, severe dizziness, severe dizziness Cardiac system: difficulty breathing or eating Gastrointestinal system: diarrhea Skin and subcutaneous tissue disorders: skin rashes Renal and urinary disorders: Urticarial rash

The influenza virus can resist the drug causing a decrease in the effectiveness of its dose, due to the substitution of a histidine for a tyrosine at position 275 of the NA gene. This mutation does not affect susceptibility to zanamivir since the NA molecule has a different genetic basis. Therefore, there are other antiviral treatments that are not as widely used, for example ribavirin, which inhibits iniosine-monophosphate, oligonucleotides that interfere with viral RNA translation, interferon inducers and nonstructural protein gene (NS1) inhibitors. It has also been suggested that the combination of antivirals can be administered, but there is scientific evidence on their effectiveness against influenza virus (Swierczynska et al., 2022).

Phenolic compounds in fruit peels

In order to search for natural and alternative sources of antiviral drugs and considering that pharmaceuticals require the incorporation of natural and efficient compounds for the reduction of these microorganisms, food matrices, including fruit peels, have been sought as a better option to obtain compounds that help against the influenza virus. These by-products represent alternatives for research and industrialization, preventing them from being discarded and causing a negative impact on the environment. Thus, their use aims to recover their economic value through reuse, remanufacturing, redesign and recycling with the possibility of generating different alternatives in different areas (industry, cosmetics, pharmaceuticals, wastewater remediation) (Sadef et al., 2022). Table 4 shows the percentage of fruit peel, which represents about 50% of the total weight, so it can be considered a valuable and profitable resource for obtaining PC for clinical purposes. Multiple publications have reported the identification of different PC (Table 4), including hydroxybenzoic and hydroxycinnamic acid derivatives, as well as flavonoids with one or a high degree of polymerization of hydroxyl groups or functional derivatives (esters, methylates, glycosides) (Ninfali et al., 2020). For this reason, fruit peels have been awakening a great interest for their beneficial properties that they could exert on human health, among which this article focuses on the antiviral properties.

Table 4. Phenolic compound profile in fruit peels.

Fruit		Non-flavonoids		Flavonoids
		Hyddroxybenzoic acid	Hydroxycinnamic acid	
Star fruit	*Averrhoa carambola*	ND	Ferulic acid, coumaric acid,	Catechin, epicatechin, myricetin, quercetin, apigenin
Coconut	*Coco nucifera L.*	Gallic acid	Ferulic acid, caffeic acid	Procyanidin B1, (+)-catechin
Orange	*Citrus sinensis*	Benzoic acid, p-hydroxybenzoic acid, gallic acid, vanillic acid, syringic acid	o-coumaric acid, chlorogenic acid, caffeic acid, cinnamic acid, ferulic acid, rosemarinic acid	Myricetin, quercetin, naringin, kaempferol, catechin
Grape	*Vitis vinífera L.*	Ellagic acid, quinic acid, protocatechuic acid glucoside, p-hydroxybenzoyl glucoside,	Caffeoylshikimic acid, caftaric acid and derivate, cis-coutaric acid, trans-coutaric acid, coumaric acid and derivate, cinnamic acid	Cyanin chloride, epigallocatechin, epicatechin, naringenin, quercetin and derivate, rutin, isorhamnetin, myricetin, delphinidin-derivates, cyanidin-3-monogalactoside, cyanidin-3-monoglucoside, malvidin-3-monoarabinoside, petynidin-3-monoglucoside, peonidin-3-monogalactoside, eriodictyol-glucoside, taxifolin
Lychee	*Litchi chinensis Sonn*	Gallic acid	Chlorogenic acid, caffeic acid	Catechin, rutin, epicatechin, procyanidin B2 and A2
Rambután	*Nephelium lappaceum L.*	Gallic acid, protecatechuic acid, syringic acid	Ellagic acid derivatives, chlorogenic acid, caffeic acid	Geranin, corilagin, apigenin, catechin, rutin, ellagictannin
Passiflora fruits	*Passiflora edulis Sims*	Gallic acid derivatives	ND	Epicatechin
Jackfruit Yaca	*Artocarpus heterophyllus Lam*	Vanillic acid, heptyl ester	Caffeic acid, chlorogenic acid, coummaric acid and derivate, ferulic acid and derivate, hydrocinnamic acid	(–)-Epigallocatechin 3-O-gallate, phloretin-2-O-xylosyl-glucoside, quercetin and derivate
Papaya	*Carica papaya L.*	Gallic acid derivatives, protecatechuic acid derivatives	Ferulic acid and derivatives, caffeic acid and derivatives	Quercetin, myricetin, kaempferol
Pomegranate	*Punica granatum*	Gallic acid, ellagic acid	Quercetin, kaempferol and luteolin glycosides, coumaric acid	Rutin, quercetin, punicalagin derivative, kaempferol derivative, cyanidin and derivate, hesperidin, syringetin hexoside, ellagitannins, punicalagin, anthocyanins and derivates
Mango	*Mangifera indica L.*	Quinic acid, gallic acid derivatives, 2,3-Dihydroxybenzoic acid, 4-Hydroxybenzoic acid 4-O-glucoside, 2-hydroxybenzoic acid, gallagic acid, ellagic acid, syringic acid, protocatechuic acid	Cinnamic acid, caffeic acid derivatives, ferulic acid derivatives, p-coumaric acid derivatives, chicoric acid, verbascoside, chlorogenic acid	Galloyl-A-type procyanidin dimer, mangiferin and derivative, quercetin and derivatives, catechin derivatives, epicatechin, hesperidin and derivatives, chrysoeriol derivatives, luteolin derivatives, myricetin and derivatives, kaempferol derivatives, rhamnetin and derivate, fisetin, cyanidin and derivate, 4-O-methyldelphinidin 3-O-d-glucoside, delphinidin 3-O-sambubioside, Isopeonidin 3-O-arabinoside, delphinidin and derivate, pelargonidin 3,5-O-diglucoside

Fruit		Non-flavonoids		Flavonoids
Avocado	*Persea americana Mill.*	Quinic acid, Syringic acid, vanillic acid, protocatechuic acid, p-hydroxybenzoic acid, syringic acid	Caffeic acid, p-coumaric acid, ferulic acid, sinapic acid, chlorogenic acid, sinapinic acid	Catechin, epicatechin derivative, quercetin derivative, apigenin, kaempferol derivative, procyanidin dimer A, Procyanidin trimer B-isomer 1, Procyanidin dimer B1, Procyanidin trimer B- isomer 2, diosmin
Banana	*Musa paradisiaca*	Gallic acid, quinic acid, protocatechuic acid,	Caffeic acid, cinnamic acid, chlorogenic acid, ferulic acid,	Quercetin, catechin, chyrsin, rutin,
Pineapple	*Garcinia mangostana*	Gallic acid, catechol, syringic acid	Chlorogenic acid, caffeic acid, o-coumaric acid, ferulic acid, cinnamic acid	Myricetin, quercetin, kaempferol, apigenin
Lemon	*Citrus limon*	Benzoic acid, p-hydroxybenzoic acid, gallic acid	o-coumaric acid, chlorogenic acid, caffeic acid, cinnamic acid, ferulic acid, rosemarinic acid, p-coumaric acid	Myricetin, quercetin, naringin, kaempferol, catechin, rutin
Mandarine	*Citrus reticulata*	ND	Kaempferol, luteolin, quercetrin, rhoifolin, narigenin, porcirin, neohesperidin, hesperidin, naringin, taxifolin, eriocitrin, sinensetin, nobiletin, diosmetin, didymin	ND

ND: not detectable.

Antiviral activities of PC and their importance in pharmacology

Several experimental studies have sought to find the effectiveness of the antiviral activity of PC by inhibiting the genetic material of influenza virus. Catechins can minimize the infectivity of influenza A and B viruses in kidney cells and inhibit the interaction of the virus with the cell membrane when it invades a cell (Kuzuhara et al., 2009). Bang, et al. (2018) found that nepitrin, 6-hydroxyluteolin 7-O-β-D-glucoside and homoplantaginine from *Salvia plebeia* at concentrations of 50 μM inhibited NA, suggesting that the effectiveness is given by the hydroxyl group at C-5' and methoxyl at C-6. Also, these PC are able to inhibit the endonuclease activity of virus RNA polymerase (Kuzuhara et al., 2009). PC extracts from green tea-derived by-products suppress influenza virus replication in chickens and mice when supplied at concentrations of 10 g/kg (Lee et al., 2012). Flavonoids and certain tannins have also been reported to exhibit antiviral efficacy against respiratory syncytial virus, Flaviviridae, Retroviridae, Hepadnaviridae, Herpesviridae, Adenoviridae, Orthomyxoviridae y Picornaviridae (Ninfali et al., 2020; Steinmann et al., 2013).

On the other hand, there are other flavonoids called haloflavanes, which have been little studied but have begun to be of interest due to their interest as antiviral agents. These compounds are synthetic flavonoids with the purpose of obtaining improvements in the pharmacological properties of non-fluorinated natural flavonoids. Few studies have shown that the incorporation of chlorine can significantly modulate the properties of

a bioactive molecule, increasing the bioavailability of the compound by changes in its solubility, lipophilicity by trifluoromethyl grouping, metabolic stability, conformation, blocking in a biochemical mechanism by forming hydrogen bridge bonds, stabilizing peptide bonds, modification in the reactivity of adjacent functional groups by delaying enzymatic degradation (Badshah et al., 2021). As an example, chrysin is a flavone with great antiviral properties, however, it has low water solubility, poor absorption and is metabolized at high speed, which makes it difficult to exert effects via the intestinal/hepatic route. However, fluorinated derivatives of chrysin significantly changed the pharmacokinetic and pharmacodynamic properties by increasing the biological activity (Zhu et al., 2019). 4',6-dichloroflavane is a potent inhibitor of rhinovirus; as well as other halogenated flavanes that have been shown to have in vitro antiviral activity against poliovirus type 2, hepatitis A virus and astrovirus (Badshah et al., 2021). Therefore, ongoing studies with haloflavonoids will be key to providing a better understanding of their beneficial role in human health care.

Conclusions

The search for possible integrative strategies to prevent and reduce the spread of influenza. In this sense, fruit peel presents relevant antiviral activity, which could provide an opportunity to contribute to face this disease as a supplement or as a matrix to isolate phenolic compounds for the development of new drugs for the welfare and usefulness to society. In addition, opening studies to fluoroflavanes that allow us to approach the path of research to propose its possible pharmaceutical application in the future with the support of systematized research. Finally, *in vivo* assays are required to evaluate the effectiveness of the antiviral activity of phenolic compounds, as well as the effects and toxicity they may cause.

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Cáscaras de las frutas como transporte de compuestos fenólicos con actividad antiviral de la influenza

Cáscaras de fruta como portadoras de compuestos fenólicos con actividad antiviral contra la gripe

Gilberto Mercado Mercado
https://orcid.org/0000-0002-7631-0676
Universidad Autónoma de Ciudad Juárez | Departamento de Ciencias Químico Biológicas | Juárez | México
gilberto.mercado@uacj.mx
Licenciado en química con master en ciencias químico biológicas y Ph D en ciencia en los alimentos. Miembro del Sistema Nacional de Investigadores e Investigadoras del CONAHCYT México. Experiencia en química, tecnología y bioquímica de los alimentos funcionales.

Delia Libier Hernández de la Rosa
Centro Universitario Tecnológico de Enfermería | Licenciatura en Enfermería | Tepic | México
libier_hdez@hotmail.com
Licenciada en nutrición y master en nutrición clínica. Experiencia en nutrición con pacientes con patologías renales, obesidad y crónico degenerativas.

Resumen

La influenza es un virus que infecta las vías respiratorias causando altos índices de mortalidad. Existen alrededor de 100 cepas de este virus, siendo los más frecuentes Rhinovirus y Coronavirus. Las cáscaras de las frutas son estudiadas debido a la cantidad de compuestos fenólicos (PC) con múltiples funciones positivas a la salud. Existen pruebas que los PC tienen un gran potencial antivirales. La eficacia de la actividad antivírica dependen de la hidroxilación, la metoxilación y la alquilación de varios componentes del anillo del PC. Quercetina, ácido gálico, epigalocatequina, catequina son algunos PC que se les han comprobado su actividad contra el virus de la influenza, bloqueando la entrada en las células huésped. Los haloflavanos son flavonoides sintéticos han empezado a ser de interés por sus propiedades farmacológicas como agentes antivirales. Estos compuestos con el fin de obtener mejoras en las de los flavonoides naturales no fluorados. La gran variedad de mecanismos de acción de los PC contra las infecciones víricas podría aplicarse como estrategia de tratamiento farmacéutico natural. La presente revisión pone de manifiesto analizar la importancia de las cáscaras de las frutas como materia enriquecido de PC con potenciales propiedades antivirales sobre el virus de la influenza.
Palabras clave: actividad antiviral; influenza; gripe comn; cáscara; compuestos fenólicos.

Resumo

A influenza é um vírus que infecta o trato respiratório, causando altas taxas de mortalidade. Existem cerca de 100 cepas desse vírus, sendo as mais frequentes o Rhinovirus e o Coronavirus. As cascas de frutas são estudadas devido à quantidade de compostos fenólicos (CP) com várias funções positivas para a saúde. Há evidências

de que os PCs têm grande potencial antiviral. A eficácia da atividade antiviral depende da hidroxilação, metoxilação e alquilação de vários componentes do anel do PC. A quercetina, o ácido gálico, a epigalocatequina e a catequina são alguns PCs que comprovadamente têm atividade contra o vírus da gripe, bloqueando a entrada nas células hospedeiras. Os haloflavanos são flavonoides sintéticos que se tornaram interessantes por suas propriedades farmacológicas como agentes antivirais. Esses compostos visam a obter melhorias em relação aos flavonoides naturais não fluorados. A ampla variedade de mecanismos de ação dos PCs contra infecções virais poderia ser aplicada como uma estratégia de tratamento farmacêutico natural. A presente revisão destaca a importância das cascas de frutas como um material enriquecido com PCs com possíveis propriedades antivirais contra o vírus da gripe.
Palavras-chave: atividade antiviral; vírus da gripe; resfriado comum; casca; compostos fenólicos.