Received: 16 June 2020 | Revised: 22 June 2020 | Accepted: 24 June 2020

DOI: 10.1002/ptr.6807

LETTER TO THE EDITOR

WILEY

Achyrocline satureioides (Lam.) D.C. as a potential approach for management of viral respiratory infections

Dear Editor,

Achyrocline satureioides (Lam.) D.C., Asteraceae, popularly known as "marcela," is an annual herb of South America (Ferraro et al., 2008), and inflorescence infusions have been widely used in folk medicine as digestive, eupeptic, antidiarrheal, antiseptic, anti-inflammatory, and for the treatment of flu, colds and other respiratory problems (Mendieta et al., 2015; Retta, Dellacassa, Villamil, Suárez, & Bandoni, 2012).

Sabini et al. (2012) reported that cold and hot aqueous extracts of *A. satureioides* (respectively, at 200–800 mg/ml and 200–400 mg/ml) showed antiviral activity against Western equine encephalitis virus (*Alphavirus* genus, *Togaviridae*), an enveloped positive-sense single-stranded RNA virus. Both extracts showed strong inhibitory activity after virus penetration and exhibited a slight virucidal action with lower efficacy than their antiviral properties. Furthermore, three spray-dried extracts (62.5 μg/ml) of *A. satureioides* prepared with 50% of hydroethanolic extract rich in flavonoids (quercetin, luteolin, and 3-*O*-methylquercetin) and 50% of blends of different adjuvants (polysorbate 80, colloidal silicon dioxide, microcrystalline cellulose and/or β-cyclodextrin) presented antiviral action against different strains of herpes simplex virus (HSV-1), a double-stranded DNA virus. Studies concerning the mechanism of the antiherpetic activity demonstrated that this species is able to impact the late stages of viral cycle (Bettega, Teixeira, Bassani, Barardi, & Simões, 2004). In accordance, the infectivity of pseudorabies virus (*Herpes suis*), another DNA virus, in Vero cells was decreased by an alcoholic extract of *A. satureioides* at a concentration of 35 μg/ml (Zanon, Ceriatti, Rovera, Sabini, & Ramos, 1999).

It is worth mentioning that aqueous extract from *A. satureioides* also showed immunomodulatory properties (Consentino et al., 2008; Santos, Ripoll, Nardi, & Bassani, 1999). Puhlmann, Knaus, Tubaro, Schaefer, and Wagner (1992) isolated from a cold aqueous macerate (−4°C), two metallic ion-containing pectic polysaccharides with MW of 7,600 or 15,000; both polysaccharides showed a robust in vitro anticomplementary effect, and the last one also showed anti-inflammatory activity and induced in vitro phagocytosis. These properties demonstrate that it is possible to obtain *A. satureioides* derivatives products presenting complementary effects, antiviral, and immunomodulatory.

Nowadays, it is impossible to know exactly which active compounds are involved with the detected antiviral activity of *A. satureioides*. However, phenolic compounds, especially quercetin, luteolin and 3-*O*-methylquercetin, can be considered as potential candidates. Interestingly, quercetin and its derivatives showed antiviral activity against several viruses, such as rhinovirus, influenza virus, herpes simplex virus type 1 and coronavirus. Rhinovirus, a single-stranded RNA virus from the *Picornaviridae* family, is a major cause of common cold. Rhinovirus infections are related to mild disease representing an economic problem, such as loss of working and school periods, and most importantly, they can trigger asthma and chronic obstructive pulmonary disease exacerbation. The incubation of airway epithelial cells with quercetin 6 hr after rhinovirus infection decreased the viral load impacting both stranded viral RNA synthesis and capsid protein levels. Besides the in vitro findings, the treatment with quercetin (gavage, 0.2 mg of quercetin daily) reduced rhinovirus replication and the expression of chemokines and cytokines in mice infected with this virus (Ganesan et al., 2012). Accordantly, Farazuddin et al. (2018) reported that quercetin supplementation (diet containing 0.1% quercetin) diminished rhinovirus-induced exacerbation of lung disease in a mouse model of chronic obstructive pulmonary disease.

Uchide and Toyoda (2011) suggested that quercetin could reduce the lethality rates from severe complications related to pandemic influenza A (H1N1) virus infection. In this context, quercetin was also able to inhibit the early stages of influenza infection caused by several strains of influenza, such as H1N1 and H3N2, which have negative-sense single-strand RNA genome (Wu et al., 2016). Interestingly, quercetin supplementation also reduced influenza infection in mice (Davis, Murphy, McClellan, Carmichael, & Gangemi, 2008).

A systematic review and meta-analysis showed that single- or double blind randomized controlled trials bring evidence regarding flavonoid supplementation effects on upper respiratory tract infections (URTI). Flavonoid supplementation, ranged from 0.2 to 1.2 g/day and including anthocyanins, isoflavones and quercetin, was able to reduce URTI incidence, and an unclear reduction in URTI sick days was described as well (Somerville, Braakhuis, & Hopkins, 2016). Heinz, Henson, Austin, Jin, and Nieman (2010) reported the effects of quercetin supplementation (500 and 1,000 mg/day) for 12 weeks on URTI rates in a double-blinded, randomized, placebo controlled trial; middle aged and older subjects (1,000 mg quercetin/day) showed a significant reduction in URTI total sick days and severity.

It is remarkable to note that quercetin in vitro inhibited a murine coronavirus, mouse hepatitis virus (Chiow, Phoon, Putti, Tan, & Chow, 2016). It was demonstrated that several quercetin derivatives were able to interact with the bounding pocket of SARS-CoV 3C-like protease, which is one of the most promising targets for the discovery

of drugs with antiviral action against the replication of coronaviruses (Chen et al., 2006).

Although it is impossible to assume that recently preconized scientific qualitative standards for plant-derived products, such as acceptable doses/concentrations, have been achieved completely in here described in vitro and vivo studies (Heinrich et al., 2020), taken together it is reasonable to infer the potential antiviral of *A. satureioides*, the relationship between composition (specifically phenolic compounds, quercetin, and polysaccharides) and mechanisms of action (inhibiting the viral 3CL protease and immune modulation, respectively).

In this context, *A. satureioides* and quercetin can be suggested as alternative approach for management of viral respiratory infections, including the new respiratory virus outbreak and pandemic, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV2), by their antiviral and immunomodulating effects.

ACKNOWLEDGMENTS

The authors acknowledge the Brazilian funding agency CNPq (MCTI) for their research fellowships.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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