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Development of enhanced buccal films with *Actinidia arguta* fruit extract for oral mucositis prevention: from *in vitro* buccal models to *ex vivo* investigations

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Abstract

Background: Oral mucositis (OM) is a common side effect of cancer treatments such as chemotherapy [1], being characterized by disruption of the oral mucosa integrity, inflammation, and pain [1,2]. The treatment strategies to prevent and treat OM are still unsatisfactory, leading to the search of new active compounds, particularly from natural sources, such as *Actinidia arguta* fruits [1]. *A. arguta* fruit, commonly known as kiwiberry, has been associated with different therapeutic properties and pro-healthy benefits, particularly antioxidant, anti-inflammatory and anticancer effects [3,4], due to the fruit's outstanding content in phenolic compounds, vitamins, and organic acids [3,4]. **Objective:** The aim of this study was to develop buccal films with *A. arguta* fruit extract as active ingredient to prevent OM symptoms. **Methods:** The films were prepared by solvent casting employing 1% of HPMC K100 LV EP, 2.5% glycerin, and *A. arguta* extract as solvent, previously prepared by Ultrasound-Assisted Extraction [4]. **Results:** Different films parameters were assessed, namely physical features (weight: 194.8 mg; thickness: 0.37 mm; disintegration time: 15.05 min; moisture content: 10.53%; swelling capacity: 55.95%), mechanical properties (resistance to extension: 10.11 N; percent of elongation: 36.10%; Young's modulus: 0.0034 MPa) and antioxidant/antiradical activities (TPC = 6.46 mg GAE/g film; FRAP = 49.45 µmol FSE/g film; ABTS = 3.74 mg AAE/g film; DPPH = 4.90 mg TE/g film). *In vitro* cell assays attested the absence of negative effects on HSC-3 and TR146 oral cell lines. Most important, the compounds release profile was assessed through *in vitro* cell models (TR146) and *ex vivo* assay with porcine mucosa coupled to LC/DAD-ESI-MS quantification. The results revealed high permeation of rutin (88.32%), quercetin-3-*O*-glucoside (84.95%) and catechin (79.74%). **Conclusions:** Overall, these results highlight the significant potential and safety of buccal films with *A. arguta* fruit extract to prevent OM condition.

Keywords: *Actinidia arguta*; buccal *in vitro* model; porcine mucosa *ex vivo* assay; antioxidant compounds; oral diseases

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