ANTI-INFLAMMATORY AND ANTIOXIDANT ACTIVITY OF ALOE VERA GEL AND PUNICA GRANATUM: ONCONUTRACEUTICAL POTENTIAL IN INTESTINAL EPITHELIAL CELLS

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Introduction: Intestinal epithelial cells (IECs) play a pivotal role in maintaining intestinal homeostasis. Different noxious agents, such as chemical, physical, infectious, and inflammatory injuries can damage the intestinal epithelial integrity. This damage results also to be associated to anticancer therapies. Chemotherapy not only targets cancer cells, but also normal rapidly dividing cells, especially those lining the gastrointestinal tract. Gastrointestinal mucositis is a frequent and severe side effect of chemotherapy and radiotherapy in cancer patients. These effects result in an overproduction of pro-inflammatory and pro-oxidant factors. The release of pro-inflammatory factors, such as cycloxygenase-2(COX-2), inducible nitric oxide synthase (iNOS) expression, cytokines and chemokines, as well as oxidative stress, with the release of reactive oxygen species (ROS), are the main events taking place in mucositis. Currently, no effective treatments exist for chemotherapy-induced mucositis, prompting the need to develop anti-mucositis agents for the use in clinics. Aloe vera is a cactus-like plant that grows readily in hot climate and it belongs to the Liliacea family. Only two species are grown commercially: Aloe barbadensis miller and Aloe aborescens. The parenchymatous cells in the fresh leaves of Aloe vera secrete mucilaginous gel that contains 98-99% water and 1-2% active compounds. Punica granatum is the fruit of the pomegranate tree, apparently to the Punicaceae family. Several evidences indicated the beneficial effects of Punica granatum to counteract several chronic inflammatory and oxidative stress state, mainly for its high polyphenol content. In this study we investigated the effects of Aloe barbadensis alone and in combination with Punica granatum in a model of oxidative stress and inflammation in IEC-6cell line.

Materials and methods: Intestinal epithelial cells (IEC-6) were incubated with Aloe barbadensis (100-12.5μg/mL) alone or in combination with Punica granatum (in 9:1ratio) for 1h and then simultaneously to peroxide hydrogen (H_2O_2; 1mM) or to Lipopolysaccharide from E.coli (LPS; 1μg/mL) plus Interferon-γ (IFN-γ; 10 U/mL). ROS intracellular production was evaluated by the probe 2′,7′-dichlorofluorescein-diacetate. COX-2and iNOS expression as well as Heme Oxygenase 1(HO-1) and NAD(P) H Quinone Dehydrogenase 1(NQO1) expression were evaluated by cytofluorimetric tecniques.

Results: Aloe barbadensis inhibited ROS production at the higher tested concentrations both in oxidative stress and in inflammatory conditions ($P<0.05$vs H_2O_2/LPS) as well as COX-2and iNOS expression at all tested concentrations ($P<0.05$vs LPS), in inflammatory conditions. In this experimental condition Aloe barbadensis also increased the expression of the cytoprotective enzymes such as HO-1and NQO1. The IEC-6treatment with Aloe barbadensis and Punica granatum (9:1ratio) significantly increases the anti-inflammatory and the anti-oxidant response respect to Aloe barbadensis alone.

Discussion and conclusion: Our results indicate that Aloe vera gel and Punica granatum combination could be useful to reduce the oxidative stress and inflammatory-mediated complications associated to chemotherapy, as mucositis, at intestinal level.