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a reduction of the final tumor volume (p = 0.03) and an overexpression of VASH (p = 0.03), but without affecting the vascular amount (p > 0.05). When administered therapeutically, all the tested compounds were able to inhibit tumor growth (p < 0.01), assuming that the Q3G group had decreased final tumor volume (p = 0.04) as well as increased VASH expression (p = 0.03) and decreased vascular proliferation (p < 0.05). It was found an inversely proportional relationship between the tumor growth of human colon adenocarcinoma/HT-29 and VASH expression (p < 0.05).

Conclusion: Flavonoids HR and Q3G demonstrated antiangiogenic potential in colon adenocarcinoma/HT-29 when administered prophylactically and therapeutically, respectively. Q3G showed direct inhibition of the neovascular proliferation. No conflict of interest.

Flavonoids Q3G and HR demonstrated antitumor activity. Reduction of tumor growth was observed in all groups, moreover it was directly proportional to the reduction in mutated p53 expression in the therapeutic Q3G group (p = 0.03), indicating a potential pro-apoptotic action and cell cycle arrest (G1 / S phase) through p53 signaling pathways. No conflict of interest.

### Flavonoids Q3G and hydrolyzed rutin demonstrated antitumor activity in a colon adenocarcinoma – in vivo study


Background: Flavonoids are polyphenolic compounds widely distributed in the plant kingdom, whose importance lies in its beneficial physiological effects, including antioxidant and anti-angiogenic effects. Carcinogenesis is a complex process that involves metabolic and cell proliferative changes by alteration in organic circuits, including oncogenes and tumor suppressor genes such as p53 and ING2.

Method: For the experiment, 25 athymic mice were used and randomly divided into 5 groups: control, therapeutic Q3G and HR, prophylactic Q3G and HR. All animals were implanted with colon adenocarcinoma (HT-29) tumor cell line under subcutaneous tissue. Control animals had their tumors grown as assessed and used as a standard curve for comparative analysis. Prophylactic groups were gavados with their respective drugs for 7 days prior to tumor implantation, while animals from therapeutic groups were gavados and gavados only when their tumors reached volumes equal to or greater than 100 mm³. After the evaluation of tumor growth the animals were euthanized, their tumors resected and stored for histological analysis and immunohistochemistry. The mechanism of action of the compounds was evaluated by immunohistochemical analysis of paraffin embedded tumor pieces in situ, the expression of proteins that participate in cell regulation, the process and progression of carcinogenesis, p53 and ING2. The analysis of the results was carried out by adopting a significance level of 5% (p < 0.05).

Results and Discussion: Histological analysis showed poorly differentiated adenocarcinoma with the presence of signet ring cell. There was a reduction of tumor growth in all groups tested in the control group (p = 0.00), Immunohistochemical analysis revealed a reduction in the expression of p53 (p = 0.00) in all groups compared to control group. There was no difference in the expression of ING2 (p = 0.97). The drugs tested exhibited tumor growth inhibition and involvement in antiproliferative pathways mediated by the p53 protein, corroborating literature data showing activation of apoptotic mitochrondial pathway of flavonoid.

Conclusions: Flavonoids Q3G and HR demonstrated antitumor activity. Reduction of tumor growth was observed in all groups, moreover it was directly proportional to the reduction in mutated p53 expression in the therapeutic Q3G group (p = 0.03), indicating a potential pro-apoptotic action and cell cycle arrest (G1 / S phase) through p53 signaling pathways. No conflict of interest.

### Flavonoids HR and rutin hydrolyzed by hesperinase as an alternative?

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Flavonoids have shown biological effects, including antitumor activity by cell cycle arrest, DNA repair and apoptosis induction. Quercetin-3-O-glucoside (Q3G) has been the aim of several studies; however, it is scarce compared to rutin (Rutin). Rutin is a glucoside (Q3G) has been the aim of several studies; however, it is scarce compared to rutin (Rutin). Rutin is a glucoside that has been isolated and will be used in this study. In the present study, we demonstrated that rutin could be obtained from the crude extract of Brazilian Rutin 3-rutinoside (Rutin), resulting in a mixture addressed as Hydroized Rutin (HR), with significant increase in bioavailability and antitumor potential. This study sets out to evaluate HR's cytotoxic activity in vitro, and its antiproliferative, pro-oxidative and genotoxic potential in animal model of glioma/U-251.

Methods: Tumor cell lines panel were evaluated for HR's antiproliferative activity using Sulforhodamine B assay. HR's action mechanisms were also investigated in cells apoptosis and cell cycle by flow cytometry. 15 nude mice randomly were divided in 3 groups: control (n = 7), HR treatment (n = 4) and HR prophylaxis (n = 4). All animals were grafted with human Glioma/U-251. The control group didn't receive any treatment. The HR prophylaxis group received the biocompound for 5 days prior to tumor graft, while the HR treatment group first received the graft, initiating compound administration only when tumors reached volume >100 mm³. All animals had tumor growth daily monitored. The control group was used as a standard for comparative analysis. The animals were euthanized and the tumors resected. The histopathological analysis used to confirm diagnosis, morphological characteristics, number of mitosis and the presence of necrosis. Lipid peroxidation was done by TBARS method and genotoxicity tests by COMET assay. The results were carried out adopting a significance level of 5%.

Results: Among the tumor cell lines tested, HR obtained the best antiproliferative effect on Glioma/U251, able to reach significant results of total growth inhibition (TGI) with 3.6 μg/mL of drug concentration. No results were found in apoptosis flow cytometry. However, HR showed action of cell cycle arrest in the G1 phase, demonstrating a cytostatic effect. There was tumor growth inhibition on treated (p = 0.03) and prophylaxis group (p < 0.01). There was a decrease in mitoses (p = 0.04) in the treated groups. There was an increase in lipid peroxidation of both prophylactic and therapeutic HR groups. There was no significant variation in oxidative DNA damage level.

Conclusion: HR exhibited moderate antiproliferative action in glioma. Cytotoxicity was proven by TBARS assay; although, no genotoxic effect was shown. The evaluation of possible action mechanisms of HR in glioblastoma demonstrated cytostatic effect, but no apoptosis induction. Therefore, HR presents antiproliferative effect in high grade glioma/U-251. Results suggest that mitosis reduction and cellular morphology changes are due to mechanisms related to drug action through a process of apparent oxidative damage on the cell membrane.

No conflict of interest.

### Hydrorutin in an animal model of human glioma

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Among the various types of cancers, glioma is configured as a neoplasm of high power of invasion, proliferation and recurrence, being among the most important sources of human cancers. The average survival time is usually less than one year after diagnosis. Thus, the need to search for new drug to combat this tumor improves survival of patients. Flavonoids are phenolic compounds of natural origin that are present in most foods of the human diet and have antitumor activity.