EVALUATION OF *IN VITRO* ANTITUMOR ACTIVITY AND CELL DEATH PATHWAY OF SYNTHETIC MOLECULE BASED ON THE GENUS PIPER IN ORAL SQUAMOUS CELL CARCINOMA (OSCC)

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Introduction

In traditional medicine, many plants, such as those of the Piper genus, are used in the treatment of oral squamous cell carcinoma (OSCC). Thus, isolated substances derived from these plants are often used as a base molecule for the synthesis of analogues, which may also have significant antitumor effects. The objective of this work is to evaluate the antitumor activity and selectivity of synthetic molecules based on a substance isolated from Piper in SCC9 cells of OSCC.

Material and Methods

A collection of esters and amides was prepared from 3,4,5-trimethoxybenzoic acid. Fourteen esters (RHE1, RHE2, RHE3, RHE4, RHE5, RHE6, RHE7, RHE8, RHE9, RHE10, RHE11, RHE14, RHE15 and RHE16) and eight amides (RHA1, RHA2, RHA3, RHA4, RHA5, RHA6, RHA7 and RH8) were obtained. From this, the viability assay (MTT) was performed on SCC9 and normal gingival fibroblasts, and substances with greater activity and selectivity were selected to continue in assays to determine the type of cell death.

Results and Discussion

Substances RHE5, RHE6, RHE10, RHE11 and RHE15 were the most active and selective in SCC9, with RHE11 (IC50= 68.69; SI= 53.12) being selected to continue the tests, due to its greater activity and selectivity. In addition to cell viability, it was observed that RHE11 did not show hemolytic activity in human erythrocytes. Video time-lapse microscopy of SCC9 treated with RHE11 demonstrated that these cells exhibit a morphology indicative of cell death by apoptosis. From this, flow cytometry was performed, in which an increase in annexin V+PI labeling, positive labeling of a single PI, active caspase-3/7 and an increase in sub-G0 were observed. Several studies have shown that a substance derived from the Piper genus, such as piplartine, is associated with triggering apoptosis in tumor cells [1, 2, 3].

Conclusion

All these results showed that RHE11 has antiproliferative activity and selectivity, indicating a possible cell death by apoptosis process in SCC9.

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