ABSTRACT

OBJECTIVE: PPAR-gamma agonists are thought to be useful due to their anti-inflammatory and anti-proliferative effects. These are not fully understood, however, and often need more investigation.

MATERIALS AND METHODS: Human cell lines (SCC15) with oral cavity cancer were used in this study. SCC15 cells were treated with: 10, 20, and 50 µM GW1929 (GW, vehicle used as control). Cellular proliferation was measured through the Tetrazolium salt WST-1 assay and flow cytometry was used to analyze cell cycle progression.

RESULTS

- GW1929 treatment resulted in a dose-dependent inhibition of cell proliferation across all treatment durations.
- GW1929 treatment also resulted in a dose-dependent inhibition of cell viability at all treatment concentrations.
- GW1929 treatment resulted in a significant reduction of MMP-9 mRNA levels by 36, 64, and 78% respectively.
- GW1929 treatment resulted in a significant increase of TIMP mRNA levels by 23 and 45%, respectively.

CONCLUSION: GW1929 is a new potent PPAR-gamma agonist with great potential in the treatment of oral cavity cancer.

INTRODUCTION

Oral cavity cancer is the 8th most common cancer in the world among males and the 14th among females. In the United States, 5,500 new cases of squamous cell carcinoma of the tongue (SCC) are diagnosed each year. Leukoplakia or oral hyperkeratosis is the stage before the development of SCC. Management focus has expanded to integrate the concept of molecular therapy, as more nuclear receptor modulators have gained clinical relevance.

PPAR-gamma agonists are known to induce apoptosis and inhibit cell proliferation. At 24, 48, and 72 hours, effect was seen in the following:

- GW1929 significantly decreased proliferation in SCC15 cells.
- GW1929 significantly decreased proliferation in SCC15 cells.
- GW1929 significantly increased TIMP mRNA levels.

DISCUSSION

Based on the results of this study, GW1929 has an antiproliferative effect on SCC15 cells, both dose and duration of treatment dependent. Molecular mechanism of the PPAR-gamma agonist effect remains to be elucidated. It appears that GW1929 affects both cell cycle progression, cell cycle arrest, and apoptosis. Cell cycle progression from G1 to S phase was related to proliferation between 5 and 20 µM GW1929. GW1929 also shows a mitotic arrest and possibly induces cell death in SCC15 cells.

CONCLUSIONS

We conclude that GW1929 possesses a great anti-carcinogenesis potential, as evidenced by its ability to inhibit proliferation and possibly invasiveness of squamous cell carcinoma of the tongue.