

3rd International Conference on

PROSTHODONTICS & RESTORATIVE DENTISTRY

April 16-17, 2018 | Las Vegas, USA

Novel piperidone derivatives with the potential to treat oral cancer

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Aim: The aim of the present study is to prepare novel lead compounds with CC50 values of less than 10 μ M and SI figures in excess of 10. Oral cancer accounts for 1-2% of all cancers that may arise in the body and 90% of these oral cancers are in the form of squamous cell carcinoma (SCC). Currently, the main method of management of SCC is through Mohs surgery, which is an invasive and technique-sensitive procedure. The aim of this research is to synthesize compounds that are toxic to oral SCC and also display tumor-selective cytotoxicity. The hope is to create a more effective and less invasive method for treating SCC.

Methodology: The prototypic molecule used is 3,5-bis(benzylidene)-4-piperidone (compound 1) which was synthesized by a literature procedure. From this juncture, four additional compounds, 2-5, were prepared which have different substituents on the aryl rings. These compounds were screened against three human cell lines of oral squamous cell carcinoma: HSC-2, HSC-3 and HSC-4. They were also assessed against human gingival fibroblasts, pulp cells and periodontal ligament fibroblasts which are non-malignant cells. Melphalan was used as the reference drug. From this data, the potencies and selectivity index (SI) figures (CC50 values against non-malignant cells/CC50 figures towards neoplastic cells) were determined.

Results: Among the five compounds evaluated, compound 4 was the most potent with a mean CC50 value of 0.51 ± 0.21 μ M towards the malignant cells. It has an average SI figure of 6.4. Compound 5, although having an average CC50 figure of 22.3 ± 4.3 μ M, was the most selective with a SI value of >17.2 .

Conclusions: Since compound 4 was the most potent and compound 5 was the most selective towards malignant cells, a future goal is to prepare analogs of 4 and 5 bearing in mind the structural features of these two compounds. The aim is to prepare novel lead compounds with CC50 values of less than 10 μ M and SI figures in excess of 10. Should these objectives be met, consideration for animal testing will be made.

Biography

Dania Alkhani has completed her Doctor of Dental Medicine (DMD) at University of Saskatchewan College of Dentistry. She is working as Dentist in Ottawa, Canada.

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