Effect of Curodont Application on Oral Soft Tissue Toxicity

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INTRODUCTION

Caries is the most common chronic disease of childhood.[2] Access to care continues to be a major problem for patients with untreated decay, especially those with lower socioeconomic status.[4] Providers are looking to non-invasive, less costly, and effective alternatives to help alleviate these access to care issues.[4] Intervention is often necessary for initial carious lesions in high caries risk patients before the lesion progresses, leading to cavitation of the affected tooth structure. Current non-invasive treatment options for initial carious lesions in the pediatric population include fluoride varnish (FV), silver-diamine fluoride (SDF), and more recently, Curodont Repair (CR), which utilizes the P11-4 peptide.[4] Parents have had a positive reception to this treatment option due to its non-invasive nature and relatively short treatment time.[3] Because of the esthetic concerns, parents are often quite hesitant to consent to SDF treatment as the affected tooth structure turns black.[5]

Curodont Repair Fluoride Plus is currently marketed as an alternative treatment to SDF, specifically for non-cavitated incipient carious lesions. It is a biomimetic material whose active ingredient is P11-4, a self-assembling peptide that promotes remineralization of incipient lesions. This peptide provides a matrix for remineralization in the tooth, utilizing the minerals available in the saliva.[1] CR does not stain tooth structure in the same manner as SDF. Unlike SDF, however, Curodont does not arrest carious lesions, which is a disadvantage.

During the application of CR, like SDF, there is potential contact with the adjacent gingiva, especially on interproximal lesions and smooth surface lesions at the free gingival margin. If such contact occurs, there are potential cytotoxic effects on gingival fibroblasts. If these cells are unable to survive, proliferate, migrate, and attach after the application of CR, the surrounding periodontium can be affected. This could lead to an inability for the teeth to respond to bacterial plaque (gingivitis) or affect the attachment apparatus of the tooth. There is currently no data on the soft tissue toxicity of Curodont. Hence, this study aims to evaluate the cytotoxicity of Curodont on soft tissue concerning gingival fibroblasts (GF) and to assess the survivability, proliferation, mobility, and attachment compared to SDF and fluoride varnish as controls.

METHODS

Gingival fibroblasts were established from a 13-year-old boy with no systemic diseases and healthy gingiva who underwent periodontal surgery at Louisiana State University School of Dentistry following informed consent as prescribed in an approved Institutional Review Board protocol. Cells were maintained in minimum essential medium *alpha* (MEMα) containing 10% fetal calf serum (FCS) and 200 units/mL penicillin and 200 µg/mL streptomycin. Gingival fibroblasts between the 12th and 20th passage were used for this study.

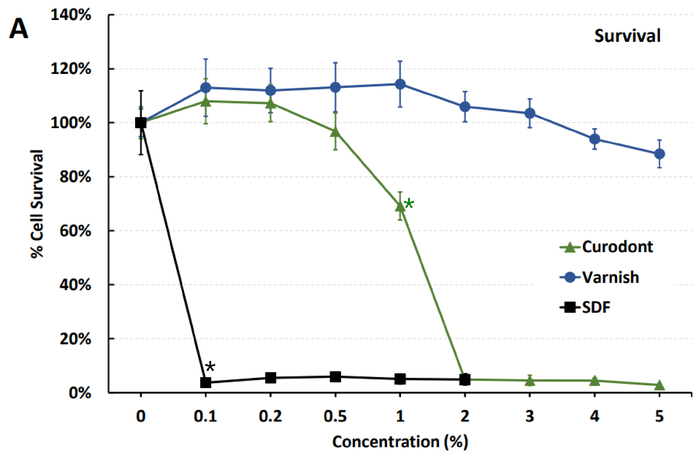
Test solutions were prepared by dissolving CR, SDF, and FV into MEMα to a stock concentration of 10%, and further dilutions of the test solutions were made using MEMα containing 10% serum and antibiotics. For cytotoxicity experiments, cells were plated into 48-well tissue culture plates and allowed to adhere for 24 hours at 37°C in 5% CO2. After 24 hours, the cell media was replaced with the test solutions. Eight samples were used for each test condition at various concentrations. Untreated cells served as controls. After 24 hours, the test condition media was replaced with media containing Calcein AM dye, the cells were incubated for 2 hours to fluorescently label cells, and living cells were quantified using a fluorescence microplate reader with filters appropriate for 480nm and 520nm emission.

For cell adhesion experiments, cells were allowed to adhere in the presence of test solutions (as above). For proliferation experiments, cells were plated as above at a low density and incubated for 1-7 days. The cells were fluorometrically labeled for quantification as above (n=8).

Statistical Tests Utilized:
- Student's T Test
- ANOVA

RESULTS

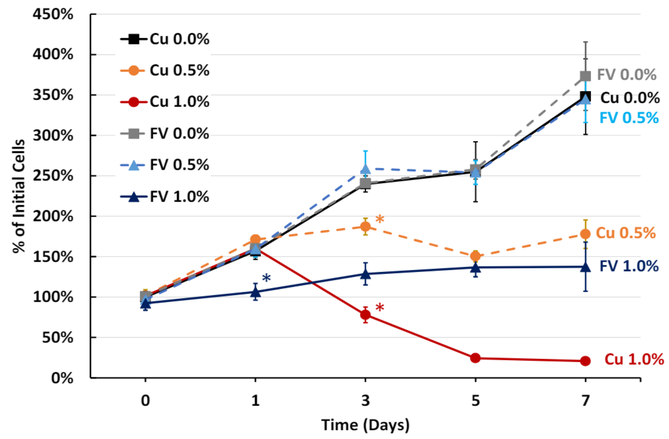
Figure 1. Cell survival after application of SDF, Curodont, and FV



Percent survival of human gingival fibroblasts (GF) after 24-hour exposure to SDF, FV, and Curodont at various dilutions.
- Significant reductions in cell survival were noted for Curodont starting at 1% and SDF at 0.1%.

(n=8) (* = P < 0.05)

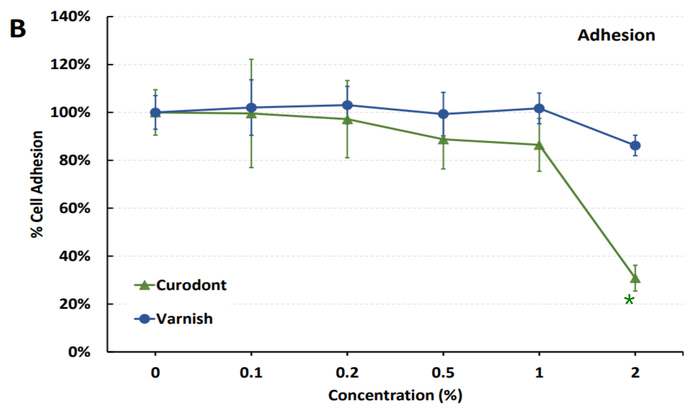
Figure 3. Cell proliferation after application of Curodont and FV



Human gingival fibroblasts (GF) proliferation after 24-hour exposure to FV, and Curodont at various dilutions.
- Significant differences were noted for Curodont starting at 0.5% and FV at 1%.

(n=8) (* = P < 0.05)

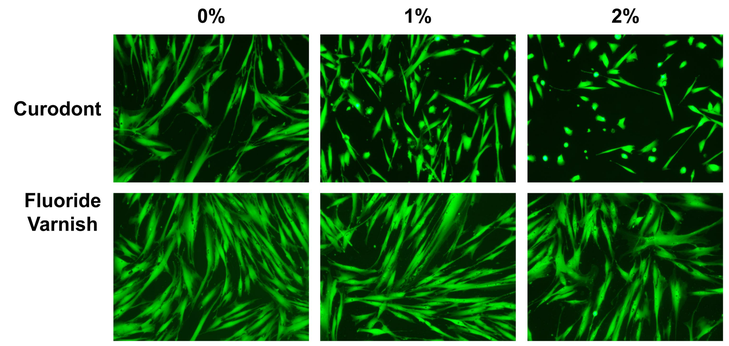
Figure 2: Cell adhesion after application of Curodont and FV



Percent attachment to tissue culture plastic of human gingival fibroblasts (GF) in the presence of FV, and Curodont at various dilutions for 24 hours.
- Significant reduction of attachment was noted for Curodont starting at 2%.

(n=8) (* = P < 0.05)

Figure 4. Cell morphology after application of Curodont and FV



Human gingival fibroblasts (GF) morphology after 24-hour exposure to FV and Curodont at various dilutions.
- Curodont led to a decrease in cell shape and attachment.
- FV led to an increase in intracellular vacuoles without a change in cell shape.

CONCLUSIONS

Based on the study's results, the following conclusions can be made:

1. Curodont is less cytotoxic than SDF.
2. Curodont is more cytotoxic than FV.
3. Curodont even at low concentrations significantly affects cell survival, cell proliferation, and cell adhesion properties.

SELECTED REFERENCES

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