**Functional Denture Materials for Rechargeable, Long-term Antifungal Drug Delivery**

Yuyu Sun
Department of Chemistry, University of Massachusetts Lowell

**Statement of Purpose:** The clinical use of dentures often leads to *Candida*-associated denture stomatitis (CADS), a common and recurring disease that affects up to 67% of denture wearers. The colonized *Candida* and other species can further cause caries, periodontal diseases, oral, gastrointestinal and pleuropulmonary infections, and even death. Antifungal dentures are used to control the disease. The most widely used approach in fabricating antifungal dentures is to impregnate denture materials with antifungal drugs that elute from the device and inhibit microbial growth. However, most of the antifungal dentures are not effective for long-term uses. A primary reason is that the current impregnating approaches cannot incorporate enough antifungals into dentures to maintain the necessary drug concentration near denture surfaces for extended uses (e.g., months to years). After days to weeks, the antifungals released cannot reach the necessary concentrations, and inhibitory effects are lost. Because dentures are often used for years and CADS is a recurring disease, long-term anticandidal denture materials that could initiate and/or stop drug release based on whether infection is present would have significant health benefits. Unfortunately, to date, this has not been achieved. To solve this problem, this study uses a "rechargeable" approach to extend anticandidal duration and mediate drug release.

**Methods:** Methacrylic acid (MAA, a monomer widely used in glass-ionomer cements and controlled drug delivery) copolymerized with acrylic-based denture resin monomers in the curing step. Physical and mechanical properties of the resulting materials were evaluated using ISO standard methods. The new MAA-containing denture materials were used to bind antifungal drugs miconazole. Antifungal activity and duration and biofilm-controlling effects of the new drug-containing denture materials were tested with *Candida* species.

**Results:** The presence of up to 10% MAA in the monomer liquid did not significantly affect water sorption/solubility of the resulting resin. Similarly, incorporating 10% MAA into the monomer liquid did not significantly affect the flexural strength/modulus of the resulting resins; with 20% or 40% MAA, however, the mechanical properties of the resulting resins were deteriorated dramatically.

Resin specimens (1x1 cm, 0.1 cm in thickness) were immersed in 2% miconazole aqueous suspension at room temperature overnight. The control (without MAA) resin absorbed 5.2 ± 0.8 μg/cm$^2$ of miconazole; the drug binding capability of the acrylic-10% MAA resin markedly increased to 41.6 ± 3.2 μg/cm$^2$ (n=5). The acrylic control and acrylic-10% MAA resin containing 41.6 ± 3.2 μg/cm$^2$ of miconazole were used for zone of inhibition and anti-biofilm studies. Figure 1A showed that the control resin had no visible inhibitory zone against *Candida*; the drug-containing acrylic-10% MAA resin produced an inhibitory zone of 3.1 ± 0.9 mm. After three days of *Candida* culture, the Scanning Electron Microscopy (SEM) image of the control resin was covered with *Candida* biofilm, but the MAA-based acrylic resin containing miconazole showed no adherent *Candid*a (Figure1 B and C).

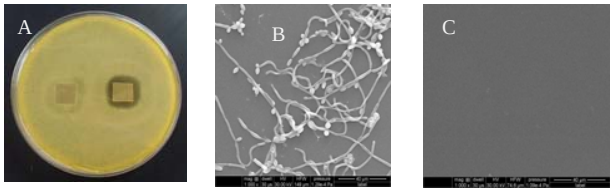


**Figure 1. (A)** Zone of inhibition of the control acrylic resin (left) and the MAA-based acrylic resin containing miconazole (right); and SEM images of **(B)** the control acrylic resin, and **(C)** the MAA-based disc containing miconazole, after immersing in *C. albicans* for 3 days.

The miconazole-containing acrylic-10% MAA resins demonstrated sustained drug release. After immersing in PBS at 37 $^o$C for 21 days (the PBS was changed daily), the resins with an initial miconazole content of 41.6 ± 3.2 μg/cm$^2$ still contained 9.12 ± 0.8 μg/cm$^2$ of miconazole (n=5), which could still provide an inhibition zone of 0.6 ± 0.2 mm. The miconazole-containing acrylic-10% MAA resins were immersed in 5% ethylenediaminetetraacetic acid (EDTA) disodium salt aqueous solution at room temperature for 8 hr; only 4.4 ± 1.7 μg/cm$^2$ of residual miconazole remained, suggesting that 89.4% of the original miconazole (41.6 ± 3.2 μg/cm$^2$) was "washed out" (quenched). The quenched resins were then recharged with miconazole by simply immersing the resins in the 2% miconazole aqueous suspension overnight, and this treatment achieved 39.3 ± 4.5 μg/cm$^2$ of recharged miconazole (n=5).

**Conclusions:** In this study, MAA copolymerized with conventional acrylic denture base resin monomers. With up to 10% of MAA, the physical/mechanical properties new resins were not negatively affected. The new resins had a much higher capability to absorb model antifungal drug miconazole than the original acrylic resins. The new drug-containing denture materials demonstrated sustained drug release for weeks. The released drugs showed potent antifungal and biofilm-formation effects against *Candida*. Drugs on the new denture materials could be "quenched" (washed out) by treating with EDTA aqueous solutions. If needed, the quenched denture materials could be recharged to reinitiate drug release.