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Activity of Three 8-Hydroxyquinoline Derivatives Against In Vitro Dental Plaque

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Three 8-hydroxyquinoline derivatives, assessed using an in vitro preformed dental plaque model system, were differentially inhibitory for four plaque-forming microorganisms.

The 8-hydroxyquinolines have been used as topical antiseptics and internal disinfectants for a number of years and apparently exhibit low toxicity for humans (2). Earlier studies demonstrated that various 8-hydroxyquinoline derivatives inhibited in vitro accumulation of the cariogenic microorganism *Streptococcus mutans* on cleaned enamel surfaces which had been repeatedly immersed in these agents (11, 12). In the study reported herein, attempts were made to determine the efficacy in vitro of three 8-hydroxyquinoline compounds, viz., 8-hydroxyquinoline sulfate (HQS; Eastman Organic), 5-chloro-7-iodo-8-quinolinol (CIQ; Pfaltz and Bauer), and 5,7-dichloro-8-hydroxyquinoline (DCHQ; Aldrich Chemical), against preformed intact plaques of pure cultures of *S. mutans* 6715-13, *S. sanguis* ATCC 10558, *Actinomyces viscosus* M-100, and *A. naeslundii* ATCC 12104. The methodology for in vitro plaque formation and the protocol for the assessment of agent efficacy have been previously detailed (7-10).

The 8-hydroxyquinoline derivatives, because they are sparingly soluble in water, were dissolved and serially diluted in polyethylene glycol 200. Other investigators have employed dimethyl sulfoxide to dissolve these compounds (11, 12). However, in these studies, such a procedure was deemed unsatisfactory because dimethyl sulfoxide was found to inhibit culture acid production, but this was not so for polyethylene glycol 200. Furthermore, polyethylene glycol, classified as a pharmaceutical necessity (6), is used extensively as a vehicle for a range of sparingly water-soluble agents, allowing their administration topically via ointment or systemically (1). In addition, there exist classes of patients for whom ointments allowing prolonged agent application to the dentition appear to be preferred vehicles (5).

Preformed plaques of the four oral microorganisms, grown to a McCabe rating of 3 (4), were immersed in various concentrations of the agents or in polyethylene glycol 200 for 30 min at 37°C. Following agent treatment, the plaques were rinsed in water twice and reincubated in a complex growth medium (3), and the production of culture acid and viability were assessed (9, 10). Table 1 indicates the concentration of the agents required to inhibit preformed plaques for an exposure period of 30 min. HQS caused cessation of culture acid production by plaques of *S. mutans* and *A. viscosus* at a concentration of 0.3%. *S. sanguis* plaques required a concentration of 3.0% to inhibit acid production, and plaques of *A. naeslundii* were unaffected by the highest concentration examined. Attempts to recover viable cells from treated plaques of cultures showing no acid production indicated that this

TABLE 1. *Concentration of 8-hydroxyquinoline derivatives required for plaque inhibition*[a]

Organism	Agent		
	HQS[b] (%)	CIQ[c] (%)	DCHQ[c] (%)
S. mutans	0.3	0.1	0.05
S. sanguis	3.0	1.0	1.0
A. viscosus	0.3	0.05	2.0
A. naeslundii	>3.0[d]	2.0	0.2

[a] Tests were run in quadruplicate. Results indicate the uniform behavior of the quadruplicate set. The agents were tested at the following concentrations (%): HQS—3.0, 1.0, 0.3, 0.1, 0.03, 0.01; CIQ—2.0, 1.0, 0.2, 0.1, 0.05, 0.02, 0.01; DCHQ—2.0, 1.0, 0.2, 0.1, 0.05, 0.02, 0.01.
[b] Bacteriostatic.
[c] Bactericidal.
[d] Not inhibitory at the highest concentration tested.

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agent was bacteriostatic for *S. mutans, S. sanguis,* and *A. viscosus* under these conditions. CIQ was bactericidal at concentrations of 0.1 and 0.05% against plaques of *S. mutans* and *A. viscosus,* respectively. *S. sanguis* plaques were killed at a concentration of 1.0%; however, this concentration was bacteriostatic for *A. naeslundii;* 2.0% was required to kill intact plaques of this microorganism. DCHQ, at a final concentration of 0.05%, was bactericidal for *S. mutans. A. viscosus* plaques required a concentration of 2.0% to effect killing, although 0.2% was bacteriostatic and inhibited acid production. *S. sanguis* and *A. naeslundii* plaques were killed at concentrations of 1.0 and 0.2%, respectively.

Thus, the 8-hydroxyquinoline derivatives were differentially inhibitory for intact plaques of the four microorganisms examined. In addition, the four test species were variously susceptible to these three agents. Thus, the in vitro data suggest that DCHQ might differentially suppress in vivo the most cariogenic of the plaque-forming organisms tested (*S. mutans*), that CIQ might differentially suppress in vivo the most periodontopathic (*A. viscosus*) of the plaque-forming organisms tested, and that HQS might suppress both. For caries-active or periodontal disease-active patients, or patients with both types of disease activity, appropriate agent choices may allow for the survival of less odontopathic members of the plaque flora (*S. sanguis* and *A. naeslundii*).

These agents are only sparingly soluble in water and thus cannot be applied via aqueous mouth-rinse vehicles. However, because they are soluble in polyethylene glycol, the possibility remains that they could be applied via an ointment with a polyethylene glycol base or in a dentifrice and thus have utility in controlling dental plaque-dependent oral infections.

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