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AH26 Releases Formaldehyde

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Formaldehyde (FA) is a normal metabolite in mammalian systems. As an example, it occurs in air as a result of automobile exhaust and combustion processes, in waste effluents, and in food.

Normally the level of free FA is very low in human tissues due to its rapid metabolism. When ingested, FA is metabolized within minutes into formic acid which is subsequently eliminated. Its half life in humans is approximately 1 h (1).

Humans are exposed to FA through dermal contact, inhalation, or ingestion. FA is irritating causing dermatitis. The true frequency of formaldehyde allergies is unknown and few data are available. Threshold values for the induction of sensitization are also unavailable. This is important as practically everyone is exposed to FA daily, but only a few persons become sensitized. Inhalation studies in rat and mice points toward an increased rate of nasal cancer (2). Humans are normally most exposed to FA through the oral route as many food groups and preservatives contain up to 10 ppm FA (3, 4). Long-term exposures to FA in rats and dogs indicate that a daily dose of 25 to 100 mg/kg body wt is tolerated without noticeable effect (5, 6). Similar high tolerance has been found when studying reproductive toxicity of FA (7). At daily doses over 100 mg/kg body wt/day for 1- to 2-yr duration, there are higher rates of intestinal tissue changes and tumors (8).

The FA content of some endodontic materials is often discussed and recently local varieties of the N2 root canal cement have been the subject of renewed interest.

When considering the high rate of exposure and tolerance of mammals to FA, the added FA load of some milligrams of FA in a root canal sealer is negligible from a toxicological point of view. Therefore, the undesirable effect of FA in an endodontic sealer cannot and should not be discussed as a general toxicity problem as this low exposure to FA is rather insignificant.

Endodontic manipulations are microsurgical procedures handling tissue areas measured in millimeters. One of the main endodontic concerns, from a prognostic point of view, is the rapid and undisturbed healing of pulp and periapical tissues. FA, even in small concentrations, is extremely reactive with proteins and effectively necrotize tissue areas in its immediate contact. It has been demonstrated (9, 10) that N2 and Riebler's paste, which are some of the more well-known endodontic sealers containing FA, coagulate and necrotize well-defined tissue areas. Thus, rapid and undisturbed healing cannot take place under such circumstances.

It has often been suggested that AH26 also contains FA which may interfere with the tissue healing process. No study of the FA content in AH26 has been done to our knowledge. The material declaration of the resin or powder components of AH26 does not list FA as a component. The powder, however, contains hexamethylenetetramine (HMT), which is synthesized from formaldehyde and ammonia. HMT also decomposes in acid environment, yielding ammonia and formaldehyde. Such decomposition can also occur in water solution. Adverse effects of high doses of HMT has not been observed in short- or long-term studies (11, 12). HMT is extensively used as an antimicrobial food additive.

This study was done to clarify the presence of FA in AH26 and the possible role of HMT as a source of FA and compare the results of similar examinations of N2 root canal filling sealer.

MATERIALS AND METHODS

The presence of FA was investigated using a gas chromatograph (H/P 5890II) and a mass spectrometer (H/P 5971A) with a direct dynamic headspace device (13). The AH26 sealer (lot 910619) and N2 (lot 2011) were mixed according to the manufacturers' directions.

The samples were weighted and immediately placed into a sample tube, which was subsequently inserted within the headspace device. The sample was moved, under computer control, into the injection port for 2 min at 150°C to release and transfer the volatiles into the GC column.

The conditions were:

Quadrex 007 FFAP 50 meters × 0.32 mm inside diameter, 3.0-μm film thickness.

Temperature program: 35 to 225°C at 15°C/min, 2 min hold at 35°C. Liquid nitrogen used to cryostat focus sample.

Thermal desorption temperature and time: 150°C for 2 min.

Mass spectrometer: 10 to 300 atomic mass units thr. 1000, A/D2 = 1.8 scans/s.

The two components of AH26 and N2 were also studied before mixing. The mixed material was studied when freshly mixed, after 12 h of chemical curing at 37°C, and after 2- and 7-day storage at 37°C and 100% humidity.

RESULTS

The findings are summarized in Table 1. N2 shows the presence of a large amount of FA molecules in the samples of freshly mixed through 2 days set samples. At 7 days the concentration had decreased to approximately one fifth of the amount found in freshly mixed N2.

The powder and resin of AH26 contains no form of FA. After mixing, however, an increasing presence of FA can be observed through the first 2 days of setting. Thereafter, the concentration decreases toward the seventh day.

TABLE 1. Gas chromatographic and mass spectrometric analysis of samples of AH26 and N2 at various setting times*

Setting Time	AH26	N2
Freshly mixed	0.12	835.00
12 hr	0.27	1740.00
24 h	1.50	1020.00
2 days	22.26	7310.00
7 days	13.39	149.00
Powder	None	Overload
Resin	None	None

* Each number represents number of ions $\times 10^6$/mg of material.

The liquid of N2 contained no FA but the content of the powder was so high that an overload of the mass spectrometry for FA occurred, making measurements impossible.

DISCUSSION

From the results, it is clear that no free FA is present in the unmixed powder or resin of AH26 despite its content of HMT. In freshly mixed AH26, FA is clearly present and the concentration has increased two-fold after 12 h into the chemical process of setting. The presence of FA increases until 2 days of setting. At this time the concentration of FA has increased to nearly 200 times over the concentration of freshly mixed AH26. The approximate setting time for AH26 is 2 days.

These results are in clear agreement with our earlier studies in vitro of the cytotoxicity of AH26 (14–16). The sealer has a relatively high toxicity immediately after mixing. This cytotoxicity decreases with time and has ceased after several days of setting. It is also easy to extract, in water, a toxic eluate from AH26 during the setting period (17). Most likely this water-soluble, transient occurrence of a cytotoxic eluate from AH26 is in effect the FA formed from decomposed HMT.

Similarly, in implantation studies we have found that freshly mixed implanted AH26 sometimes causes slight tissue necrosis. The material, however, is practically inert when implanted after setting (14).

N2 contains large amounts of FA, and during the first day the amount is more than 1000 times the amount found in AH26.

The FA in both AH26 and N2 will affect the local tissue in contact with the material. The FA dissipates into the tissue and, if concentrated sufficiently, it will cause tissue alterations and necrosis.

From biological studies both in vitro and in vivo (9, 10, 14–16) we have observed the cell and local tissue destructive effect of the FA in N2. Such severe tissue reactions are not seen associated with biological reactions to AH26 (14–17). The observation in this study showing a dramatic difference in FA content explain the differences in biological reactivity recorded.

The presence of FA in dental products must be viewed with concern, but there is no place for irrational thinking. FA, as mentioned in the introduction, is a part of our daily life and mammals normally have a high degree of tolerance to this chemical. Many dental products contain FA. Thus, the natural replacement for the amalgam restoration, composite resin, releases formaldehyde as a chemical by-product (18). Denture base materials also release FA as a by-product (19). In other sites, epithelial contact is abundant and the FA content may lead to sensitization. Such consequences are less likely when a FA-containing material is used for endodontic applications.

In endodontics, the first concern regarding a material choice must be the function of such material in the support of pulp or periapical tissue healing, without undue injury or trauma. FA, at a significant concentration, will cause tissue injury not compatible with rapid uneventful healing. N2 contains such a very high concentration, which has been repeatedly demonstrated (9, 10).

Consequently, N2 must be rejected as a rational choice of material, not due to general health risks, but due to the undisputable necrotic tissue injury caused by the formaldehyde it contains.

The tissue irritation initially caused by AH26 is most likely also caused by a low level of FA release. The concentration, however, is only a fraction of the content in N2 and the tissue will heal rapidly as the material sets, arresting further release of FA (20).

The choice of endodontic sealer is not easy as no material is available combining good physical properties with biologically inert characteristics. Despite the presence of low amounts of FA, we consider AH26 to be one of the best all around choices (16). Future research should, however, be focused on the development of an endodontic sealer with improved biological and physical characteristics.

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