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Formaldehyde and methylene glycol equivalence: Critical assessment of chemical and toxicological aspects

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ABSTRACT

Due largely to the controversy concerning the potential human health effects from exposure to formaldehyde gas in conjunction with the misunderstanding of the well-established equilibrium relationship with its hydrated reaction product, methylene glycol, the concept of chemical equivalence between these two distinctly different chemicals has been adopted by regulatory authorities. Chemical equivalence implies not only that any concentration of methylene glycol under some condition of use would be nearly or completely converted into formaldehyde gas, but also that these two substances would be toxicologically equivalent as well. A relatively simple worst case experiment using 37% formalin (i.e., concentrated methylene glycol) dispels the concept of chemical equivalence and a review of relevant literature demonstrates that methylene glycol has no inherent toxicity apart from whatever concentration of formaldehyde that might be present in equilibrium with such solutions.

1. Introduction

Until recently, regulations for occupational inhalation exposure to formaldehyde (FA) gas have been based primarily on eliminating its potential to cause sensory irritation of the eyes, nose and throat. While carcinogenic potential is mentioned, this does not rise to the level of "known" in any current workplace regulations for FA.[1] These regulations, e.g., the Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit (PEL) of 0.75 ppm and Short Term Exposure Limit (STEL) of 2 ppm for 15 min, or the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) of 0.3 ppm are based on the presumption that FA gas alone, even as it escaped from formalin solutions was the sole chemical of potential importance from a health perspective. This concern has now been expanded to include methylene glycol (MG), a different chemical and little understood component of formalin which comprises the vast majority (i.e., >99.9%) of aqueous mixtures at room temperature which can also exist in the air as a vapor.

This additional concern is due primarily to the controversy surrounding the potential health effects from the presence of MG (or other FA donors) as the active ingredient in certain products used in salons (e.g., keratin hair smoothing treatments) and the requirement for heat when such products are used. Attention about the use of these products has focused on potential FA exposure and sensory irritation of the eyes, nose and throat to either hair stylists or their customers.[2] Sporadic reports of sensory irritation occurring in conjunction with the use of hair smoothing products have been attributed solely to the presence of airborne FA gas emitted when these products are heated as part of the process. For example, an air monitoring study of FA emissions was conducted by Oregon

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[1] Other FA exposure guidelines are available but these do not carry the regulatory weight of the OSHA PEL or STEL nor are they appropriate for occupational exposures. For example, the National Institute of Occupational Safety and Health (NIOSH) Recommended Exposure Limit (REL) of 0.016 ppm is not based on health effects but rather was established as the lower limit based on analytical repeatability. Similarly, the World Health Organization (WHO, 2010) indoor air guideline of 0.08 ppm is the FA level judged protective for all potential adverse effects from 24/7 lifetime exposure. Finally, the US National Advisory Committee for Acute Exposure Guidelines (USNAC, 2008) established a FA level of 0.9 ppm for 10 min to 8 h. The NIOSH, WHO or USNAC values are not intended as FA target levels in an occupational setting.

[2] While other adverse health effects have been attributed to FA exposure (e.g., nasopharyngeal cancer and leukemia) these findings remain controversial and are beyond the scope of this report. These issues are addressed in depth in the NAS/NRC (2011) review of the EPA (2010) Draft IRIS assessment of FA as well as comprehensive reviews by Golden (2011) and Rhomberg et al. (2011). In addition, another NAS/NRC committee is presently assessing the scientific validity of the listing of FA as a known human carcinogen for leukemia by the National Toxicology Program (NTP, 2012) in the 12th Report on Carcinogens.

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OSHA (2010) in seven different salons where a single keratin treatment was conducted over the course of the day. The 8-h time weighted exposures (TWA) ranged from 0.006 ppm to 0.33 ppm while short-term (15 min, STEL) exposures ranged from 0.11 ppm to 1.88 ppm with the highest STEL below the OSHA PEL of 2.0 ppm. While none of these values exceeded the OSHA PEL several 15 min. STEL measurements exceeded the ACGIH TLV value of 0.3 ppm.

Similar findings have been reported at other salons, i.e., few exceeding the OSHA values but some in excess of the ACGIH TLV level of 0.3 ppm. For example, a recent review by Boyer et al. (2013) on the safety of FA and MG as used in hair smoothing products summarized additional air monitoring conducted in various salons and the extent to which different exposure guidelines were exceeded. While the OSHA PEL was exceeded in some instances, it is important to note, as pointed out by Boyer et al. (2013) virtually all of the emissions data summarized were based on the use of products formulated with ≈10% MG as the active ingredient. As described in the present review, with all hair smoothing products now formulated with no more than 3% MG, the FA emissions would be expected to be substantially reduced since FA in air samples is directly related to concentrations in bulk products.

As a precautionary response to concerns about the potential for hair stylist and consumer exposure to FA from MG formulated in keratin products, the Cosmetic Ingredient Review (CIR, 2011) concluded that FA and MG should be considered as essentially "equivalent" with respect to their potential to cause FA-induced sensory irritation. Shortly thereafter the European Commission (EC) Scientific Commission on Consumer Safety and the Australian Competition and Consumer Commission (ACCC, 2012) adopted similar positions. The practical consequences of the assumption of chemical equivalence between MG and FA is that, when heated under actual use conditions, any concentration of MG formulated into a product would be converted into essentially the same concentration of FA gas. This conclusion, if correct, implies not only that MG is chemically equivalent to FA but must also be toxicologically equivalent to FA as well. On the other hand, if the precautionary conclusion of equivalence was incorrect suggests that current regulatory approaches would be sufficient to prevent FA-induced sensory irritation consistent with exposure to FA in any occupational setting.

Because chemical equivalence between FA and MG implies that both are functionally identical, this review will discuss the issue of equivalence in the context of standard chemical nomenclature and the well-established equilibrium kinetics between FA and MG. In addition, newly developed experimental data are presented which demonstrate that chemical equivalence cannot be confirmed. In addition, while the toxicity of FA is well understood, because chemical equivalence between FA and MG implies toxicological equivalence as well, the potential toxicity of MG, as contrasted with that of FA, is also addressed.

2. Background

Hair smoothing products containing MG (or other FA donors or releasers) require the use of heat which affects the equilibrium between FA and MG resulting in volatilization of both FA gas as well as MG vapors. While sensory irritation of the eyes, nose or throat has been sporadically reported by both hair stylists and customers in conjunction with the use of hair smoothing products, such reports appear to be the exception rather than the rule. While hair stylists in salons are required to be trained professionals with an understanding of how to properly use such products (similar to other professional-use only products including peroxide hair color or ammonia bleaches and artificial nail products, etc.) including the need for proper application techniques and adequate ventilation, it is recognized that this may not be universally achieved. Unlike in past years when certain products contained in excess of 10% MG, these products have now been reformulated. Currently manufactured products are now formulated with no more than 3% MG, the minimum concentration required to achieve the desired effect. This also substantially reduces the likelihood of sensory irritation due simply to the presence of less MG (and therefore FA) in any given product. It is noteworthy that with the thousands of applications of these products in use each day there is a striking lack of reports from hair stylists or customers reporting the typical pungent odor of FA which often, but not always, precedes symptoms of sensory irritation (ATSDR, 1999; Golden, 2011). This suggests that such products can be used without producing sensory irritation. However, it must be noted that it is impossible to formulate a product, including those intended for purposes of hair smoothing, that cannot be misused if the above noted caveats are ignored. Hair stylists are required to follow manufacturer's instructions and to heed all label/product warnings. If this is not done then most, if not all, professional products used in salons may pose one or more potential hazards, which is why professional use products require additional appropriate training.

It is well established that the chemical equilibrium between MG and FA can be affected by heat with the potential for release of higher concentrations of FA than would occur at room temperatures. This has prompted a number of regulatory authorities to conclude, without any specific evidence, that MG and FA should be considered as chemically equivalent, i.e., that MG, under a condition of actual use would be nearly or completely converted into FA gas. This began with the Cosmetic Ingredient Review (CIR, 2011) in deliberations about the use of MG in hair smoothing products, "*. . .the ingredients formaldehyde and methylene glycol can be referred to as formaldehyde equivalents. Under any normal condition of cosmetic use, including at room temperature and above, methylene glycol is not stable in the gas phase and very rapidly dehydrates to formaldehyde and water. . . For this reason the hazards of formaldehyde equivalents in a heated solution are the same as the hazards of gaseous formaldehyde, since the solution so readily releases gaseous formaldehyde.*" This was followed by an "*Opinion on Methylene Glycol*" from the EU Scientific Committee on Consumer Safety (2012) "*. . .the formation of methylene glycol or the release of gaseous formaldehyde occurs extremely quickly. Via this dynamic equilibrium in aqueous solution, formaldehyde and methylene glycol are mutually converted and hence inherently linked with each other due to low energy barriers of formation and degradation of methylene glycol.*" As discussed in Section 5.2 the logic of this statement is demonstrably incorrect, particularly the erroneous allegation that there is a low energy barrier for the degradation of MG to FA gas implying that MG could be quantitatively converted to FA under typical use conditions. Finally, a similar conclusion concerning FA/MG equivalence was reached by the Australian Competition and Consumer Commission (ACCC, 2012), "*It is proposed that 'free formaldehyde' could be defined as 'all hydrated or non-hydrated formaldehyde present in aqueous solution, including methylene glycol*'.

None of the above cited pronouncements on FA/MG equivalence are supported by any empirical data. Rather all are based on a precautionary assumption arising from concerns that MG, under the conditions of use (i.e., heating to 400 °F) in keratin smoothing products, could release essentially the same concentration of FA into the air as was formulated into a product as MG, i.e., that any concentration of MG in a product could be nearly or completely converted to FA. If true, the inescapable conclusion of the chemical equivalence assumption would be that these two, distinctly different chemicals would be toxicologically equivalent as well. If not correct, this would suggest that MG and FA are not "equivalent" and that their potential toxicity should be considered separately.