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EMBALMING CHEMISTRY: GLUTARALDEHYDE VERSUS FORMALDEHYDE

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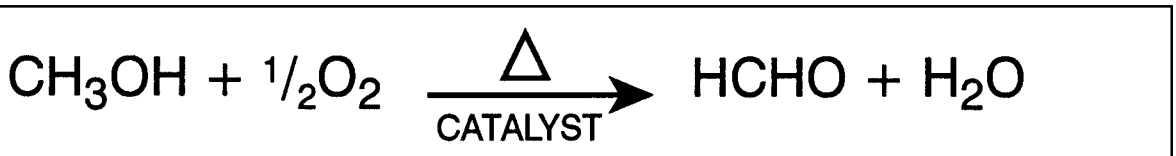
Abstract: Glutaraldehyde and formaldehyde embalming chemistry and embalming action are critically evaluated and compared. The histories of both aldehydes and their uses in related fields of interest is discussed, including tanning, histology, electron microscopy, pathology and disinfection/sterilization. Similarities of reaction and result, as well as drastic differences are catalogued and delineated. An indepth discussion of the ramifications for embalmers in conjunction with a summary completes the work.

INTRODUCTION: The following article is an indepth comparison of the formaldehyde and glutaraldehyde chemical reactivities and nuances of reaction with predominately proteins and some other related chemicals and body tissues that are of importance to embalming. The comparisons are enlightening for the similarities and the vast differences between these two reactive aldehydes in protein fixation modalities. Also covered as an important topic of discussion and use is the relative disinfection and sterilization capabilities of formaldehyde and glutaraldehyde.

There has ensued for years heated argument and discussion concerning the relative abilities of formaldehyde and glutaraldehyde as embalming agents. The debate will never end, but at least the chemical facts and fictions can be brought to light. Embalmers cannot even agree on what constitutes embalming and the relative hierarchy of reasons and justifications for embalming in the first place. By this, I refer to the relentless arguments of preservation versus sanitation versus restoration, etc, etc. In the following paragraphs I will present the reported, documented and researched chemical facts and truisms regarding these aldehydes and their relative worths in embalming. It is then up to each embalmer to make a determination and choice regarding the efficacy and validity of use of the respective agents used in embalming.

A lot of the arguments in the embalming industry regarding these fixative/reactants are based on partial information, half-truths, rumors and general shock and dismay that an old friend, like formaldehyde, is questioned or called to task for any reason, valid or not. This is a fear-driven response to a situation wherein no alternatives to formaldehyde are seen, contemplated or believed to even exist. The result is a formaldehyde-apology based industry, where nothing can be questioned or indicted for any reason, for the possible result is oblivion. This fear response is most noted when formaldehyde is called into question or reported as having exposure problems and adverse health effects. The indictment against formaldehyde in regards to exposure and health is significant and to pretend otherwise is sheer folly. Glutaraldehyde has its exposure problems and health effects also, like any hazardous chemical used in embalming. The brutal truth is, that the exposure problems associated with glutaraldehyde in embalming scenarios are but a fraction of those inextricably linked to formaldehyde – and to think otherwise is foolish. The exposure and health related characteristics of the aldehydes will not be focused upon in this investigation, however. That is a topic of enormous importance and voluminous research that has and will be covered in other reports.



MANUFACTURE OF FORMALDEHYDE
Figure 1

The focus of this report is on the theoretical and practical chemistry of formaldehyde and glutaraldehyde as primarily protein precipitants or fixatives in embalming and fixation scenarios and delineation of the advantages and disadvantages accruing to each. Formaldehyde, the embalmers ancient and deadly friend, is investigated first.

FORMALDEHYDE: The credit for the discovery and first synthesis of formaldehyde generally goes to Hofmann who passed methanol/air vapors over a hot platinum wire and documented the formation of formaldehyde in 1868. There also, is a reference to Buterov in 1859 discovering formaldehyde by the attempted synthesis of methylene glycol. At any rate, formaldehyde was relatively late in isolation and synthesis compared to the analogous aldehydes (acetaldehyde, etc.) as most attempts failed due to rapid oxidation to formic acid and reaction byproducts (HCO2H→CO2 +H20). A reasonable industrial process was introduced around 1889, wherein formaldehyde in water was produced and so-named formalin became a chemical of interest.

It didn't take long for the fixation and possible disinfection properties to become evident. Most credit Blum in 1893 with the first use of 40% formaldehyde (formalin) in histology and preservation of tissues. Trillat was also, apparently involved, with remarks in 1888 and 1891 about formaldehyde action on urine causing incorruptibility and the ceasing of putridity and decay of plants and animal parts. Blum, in working with formalins in the lab, noted that his fingers hardened and dried, like alcohols would, and then experimented with this action of formaldehyde by fixing a mouse in a 10% solution and the formaldehyde embalming industry was born. The first documented embalming of a human cadaver with formaldehyde is purported to have occurred in 1899. Over 100 years later, very little is fundamentally changed in basic chemistry or technique of formaldehyde preservation of human cadavers. For the record, formaldehyde supplanted the dangerous and toxic concoctions of heavy metal salts, that were previously used with great success, by the years 1906-1910. Formaldehyde had become then, essentially, the chemical of choice for human cadaver embalming. By the late 1950's, there was purported to be over 200 varieties and variations of formaldehyde fixative solutions with all sorts of chemical additives that could be used in various branches of pathology, histology, gross anatomy, tanning of hides and embalming of specimens.

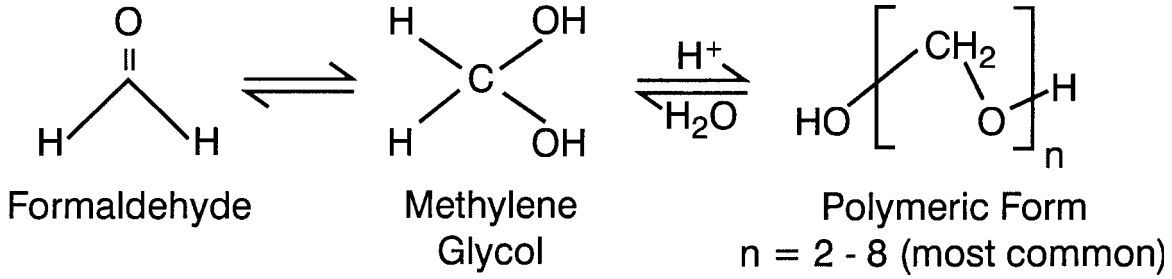
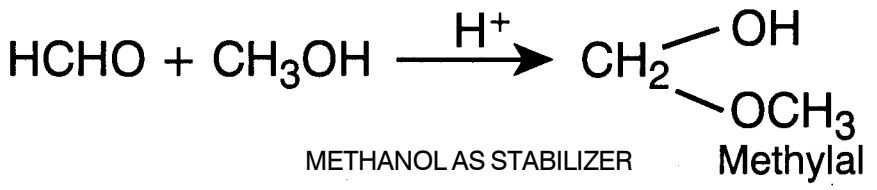


Figure 2

Modern industrial synthesis of formaldehyde is based upon oxidation of methanol over a metal catalyst (usually silver) with heat (Fig. 1). Formaldehyde is, of course, a colorless and pungently irritating gas. It is a powerful lachrimator and is explosive in air or oxygen. It is possible to liquify formaldehyde, for special circumstances of use. The vapor density is barely heavier than air at 1.06. Formalin is the chemical of commerce and is 37 to 40% formaldehyde in water by weight or volume, respectively. More dilute solutions are available and special 55% concentrations with higher alcohol content are also available. For pathology and histology uses, 10% solutions, buffered to near neutrality, are popular.

Actually, formaldehyde in formalin doesn't even exist as an aldehyde. 99.9% of formalin solutions exist as methylene glycol and its various polymers, with the true monomeric form present at only .1%.

Formalins are acidic in nature and readily form polymers of various lengths of n=2 to 100+ (Fig. 2). The smaller polymers are weak and easily hydrolyzable by acid or base hydrolysis. Polymers of n=2 to 8 are generally referred to as paraformaldehydes which exists as a white powdery solid that melts at high temperature to yield formaldehyde gas. This is a preferred way for generation of high purity formaldehyde. Aggregates of the smaller polymers can be easily hydrolyzed by water immersion and treatment by acid. The very large polymers can be difficult to hydrolyze with reaction taking weeks at a neutral pH and not much quicker even at acidic pH's. Formalin solutions are unstable and degrade if not stabilized. The most popular stabilizer is methanol at usually 3-8% in solution. Methanol rapidly forms a methylal with formaldehyde in water and is strongly favored as a reaction product (Fig. 3).



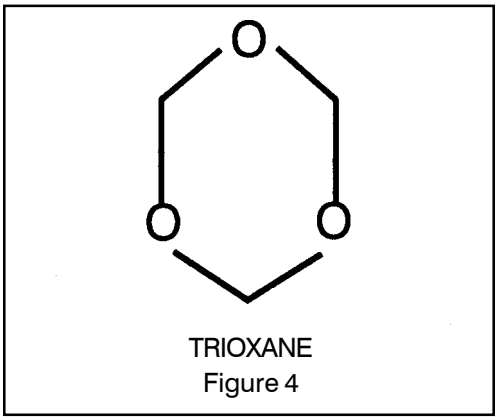
METHANOL AS STABILIZER

Figure 3

The stabilization results from an inhibition of cross-reaction and cross-addition to polymeric forms. By stabilization, up to 30% of a formalin can exist as the monohydrate methylene glycol. It is possible to utilize other stabilizers such as ethanol or even glycols or glycerine. Methanol is chosen because of its availability and it is a natural byproduct of manufacture of formalins. Other curious polymeric forms of formaldehyde can exist and be isolated, one example being trioxane, a cyclic polymer (Fig. 4). Over time, during storage, formalin solutions degrade by natural oxidation changes, caused by air or photooxidative pathways. Acidification increases, usually reaching a pH of 4 or less with the production of formic acid and formate ions. This is the reason stabilization of formalin solutions is critical. Typically, formaldehyde reactivity and polymerization increases as acidity increases, particularly at pH's of 6.5 and less. Basisity, however substantially inactivates and slows formaldehyde reactions at a pH of 8-9 and above a pH of 9 essentially non-reactive. A Cannizarro type reaction is strongly favored in very basic conditions, with a resultant loss of formaldehyde titers (Fig. 5).

Formaldehyde reaction with proteins is based on classical carbonyl-amine reaction chemistry. Amines and related nucleophiles react with formaldehyde to form various chemicals and intermediates with ultimately methylene bridging (-CH2-) resulting in fixation or tanning type action. Formaldehyde is a highly reactive carbonyl entity with no adjoining alkyl groups for stabilization, with the carbon being electrophilic and the oxygen being a nucleophilic center. Formaldehyde actually reacts as a methylene

glycol or as an unstable hemiacetal (methylal) that is strongly favored in methanolic aqueous solution. At any rate, primary amines react and form intermediate hydroxymethyl groups that drives a basisity loss with pKa drops of about 4-5 units. Subsequently, but slowly, dehydration or condensation reaction occurs by loss of a molecule of water and a methylene bridge forms (Fig. 6). Also possible, after initial reaction are dimethylene ether linkages and the reduction of hydroxymethyl groups by formaldehyde (HCHO) itself to methyl groups with production of formic acid as an endpoint product. These reducing properties of formaldehyde are accelerated in alkaline conditions where formaldehyde is known to precipitate the metals of various salts, such as bismuth, copper and silver. Basically, then endpoint reaction results are condensation with acidity promotion. Oxidation of formaldehyde can also come about spontaneously in air or with other oxidants, in addition to the hydroxymethyl groups discussed above. An interesting classical formaldehyde reaction product is that with NH3, ammonia, the reaction product being a curious cyclic, urotropin (Fig. 7).

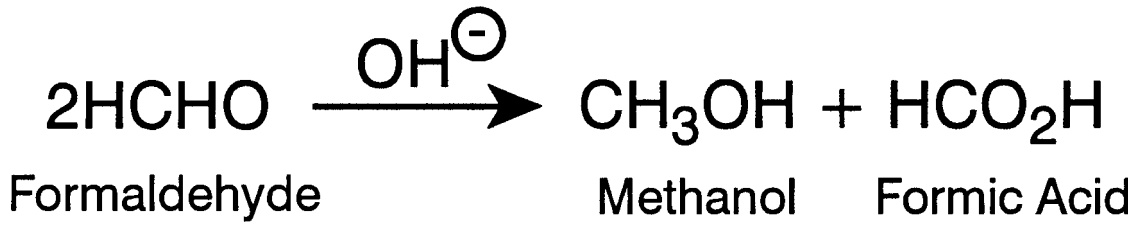


TRIOXANE
Figure 4

Specifically then, proteins present the following reactive groups to formaldehyde: terminal NH2 groupings (i.e. amines), primary amides, guanidyl groups, hydroxyls, thiols, indole nuclei, imidazolinyl and phenolic groupings. Lysine groups seem to be very preferential, probably because of conformational freedom and external surface availability as a steric effect. There are reports that thiols are not preferred and infrequently available as they are oxidized into disulfide (-S-S-) bridge linkages.

The problem with formaldehyde fixation, that has been known since 1902 is the reversibility and susceptibility to acid hydrolysis of the coagulated protein. Formaldehyde fixed gelatin was noted to be reversible by hydration and acid treatment in the very early years of formaldehyde research. In many instances, there is significant formaldehyde wash-off, i.e. unreacted or reversed formaldehyde found in post-treatment buffer wash. The amount of formaldehyde that does not wash out is reacted in a dehydration reaction. Reversing of fixation and acid hydrolysis has been know to be possible since the early 1960's by acid catalyzed hydrolysis, water immersion or heat, or a combination of the above.

The initially reversible hydroxymethyls in protein reaction, therefore, reduce by condensation reaction to hydrophobic methyls or N-formyls with formic acid formation. Methylene bridging occurs most often between lysine and various other moieties: lysine-arginine, lysine-cysteine, lysine-asparagine and lysine-glutamine and is strongly sterically controlled, occurring only when favorable proximities exist (average bonding distances being only 2 angstroms or slightly more). Dimethyl ether bridges theoretically should form but appear far fewer than anticipated.

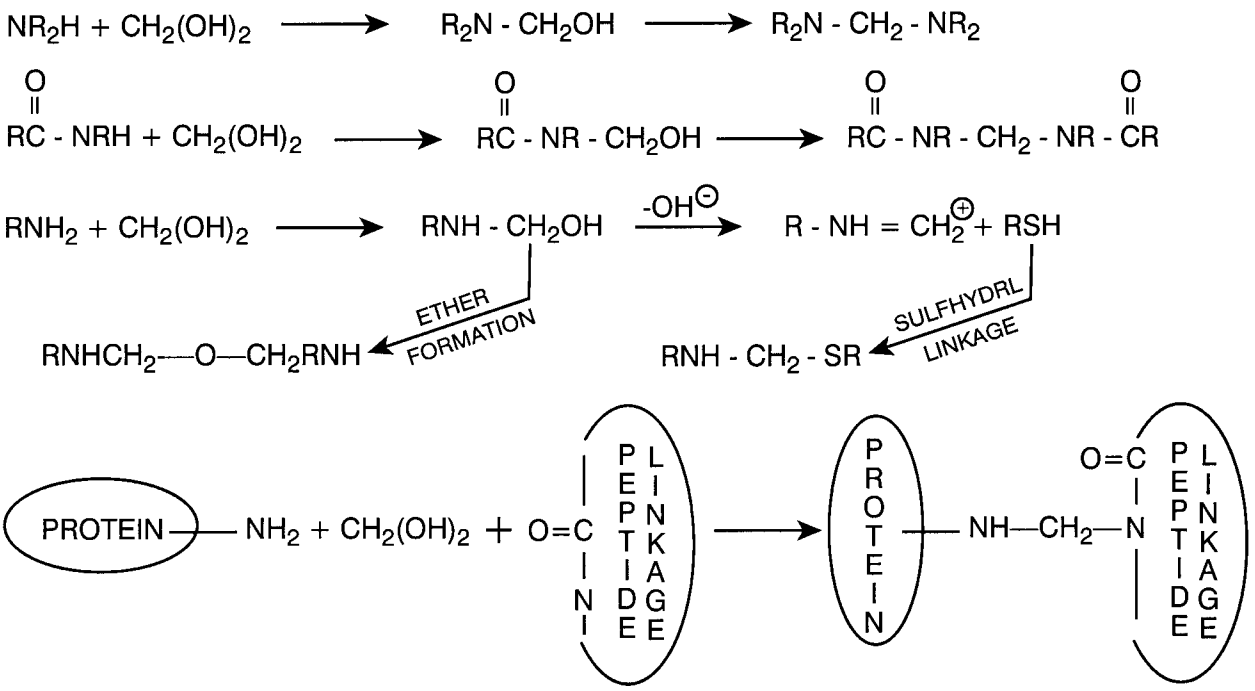


CANNIZARRO REACTION
Figure 5

In addition to the hydroxymethyl derivatives of the amine functions, guanidine, other hydroxyls, indoles and imidazoles being very unstable, certain other bridgings are also somewhat susceptible. The lysine-cysteine couplings are somewhat stable, but reversible. Lysine-arginine, lysine-asparagine and lysine-glutamine are stable but susceptible to acid hydrolysis. Lysine-tyrosine links appear to be very stable and are acid-resistant. It seems, in general that weaker and reversible links are generated during mild treatment, while strong formaldehyde treatment during fixation results in a significant amount of acid-resistant linkages. In general, pH's of 6-7 favor reversible amine reactions and pH's of 4-5.5 encourage methylene bridging. Neutral pH is not conducive to total fixation and basic pH's actually inhibit the total reaction.

Essentially, then, there are basically three competing reaction scenarios in formaldehyde fixation: 1. rapid reaction and coagulation with reversible adducts. 2. stabilized bridging but susceptible to acid hydrolysis and reversal. 3. significant endpoint bridging with high acid-hydrolysis resistance resulting in permanent fixation. The results of endpoint protein fixation are inter and intra-molecular cross-linkings causing insolubilization, trapping of various macromolecules in the fixed matrix of cross-linked proteins, dehydration and generalized hydrophobicity, and chemically induced resistance to enzyme action, microbiological interaction and chemical attack. As a side note, surprisingly and counter-intuitively, fixation does not alter the secondary structure of proteins. The more complex tertiary structures are, however, probably seriously affected by coagulation and fixation. Endpoint hardness and shrinkage of

tissues is variable and slow and occurs over days. Loss of elasticity occurs and is significant but less extreme than that associated with harsher fixative methods (heat, irradiation, acids, etc.)

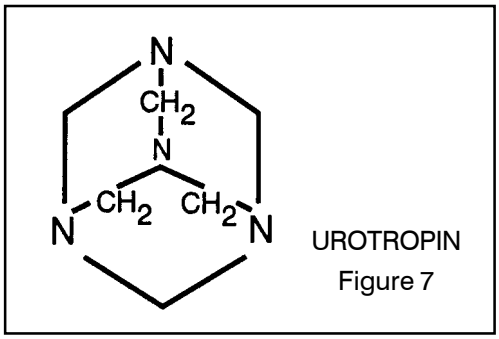


VARIOUS FIXATION REACTIONS OF FORMALDEHYDE

Figure 6

Reaction kinetics are therefore predicated on two distinct but separate modalities of reaction: 1. diffusion/penetration with resultant rapid but reversible product formation and, 2. endpoint fixation reaction that is extremely slow, but non-reversible and more or less a permanent fixation and precipitation of the protein. Reaction studies involving tagged C14 show actual endpoint reactions quite slow at moderate temperatures (25 degrees C) and a pH of 7. Typically 24 hours elapses before even equilibration occurs with only half or less of available reactive sites involved after 3+ hours. Reaction rate was essentially unchanged in a pH range of 3-8. Serious reaction rate reduction has been noted above this pH range. It is not unusual for essential complete dehydration reactions to require 7 days or longer and up to several weeks are not uncommon. If reaction times are only in hours, then only coarse reversible co-

agulation will occur. Formaldehyde penetration and diffusion into tissues can be tracked by the greying-out reaction of formaldehyde with colored organ tissues. For example, perfusion can be measured in liver tissue at 4-5mm in 4+ hours of immersion. In general, Fick's law is a good rule of thumb in these reactions with diffusion/perfusion proportional to the square of the elapsed time, in addition, to concentration and temperature considerations. Another curious color reaction of formaldehyde is with blood perfused tissues. At pH's of 6 or less, formal pigments of a brownish nature appears which probably is a hematin acid (probably linked to a reduction and deironization of heme). It has been found that neutral buffered or basic formalin does not cause this color reaction.



UROTROPIN
Figure 7

Little, if any reaction occurs with lipids, except possibly the amine group carrying phospholiplids. Non-saturated fatty acids are theoretically capable of reaction. Nucleic acids are reactive with various exocyclic bases such as adenine, guanine and cytoseine and endocyclic imines to form various adducts.

Occasionally additives are used to enhance tissue fixation and can include phenol at 2%, which accelerates fixation, reduces shrinkage and inhibits formal pigment production (essentially acting as a bleaching agent). Various salts of heavy and transition metals are very reactive and precipitate protein. ZnSO4, zinc sulfate, has been used with formaldehyde in immunochemistry preservation. Both tannic acid and mercaptoethanol have been utilized in electron microscopy as enhancers and enablers in conjunction with formaldehyde.

GLUTARALDEHYDE: The first successful synthesis of glutaraldehyde is credited to Harries and Tank in 1908. Glutaraldehyde was cataloged as a typically reactive dialdehyde and was used for various chemical syntheses of more complex chemicals in laboratories and its properties were moderately investigated. It was relatively difficult to synthesize in substantial quantities and was more a chemical of laboratory and synthetic chemistry interest. By the 1940's and 50's, it became obvious that glutaraldehyde exhibited properties that were superior in many ways to formaldehyde in protein fixation chemistry and the early field of disinfection/sterilization.

A successful method of industrial production was patented in the late 1950's by a Diels-Alder type reaction of acrolein and vinylethyl ether forming 2-ethoxy-3, 4-dihydro-2H-pyran which readily hydrolyzes to glutaraldehyde with a by product of ethanol (Fig.8). Interest in glutaraldehyde peaked in the early 1960's when several investigations found it to have outstanding disinfection and sterilization capabilities, even surpassing formaldehyde, the standard of the disinfection industry at the time. By 1963, high-level disinfectants, cold-chemical sterilants and potent sporicides were marketed with glutaraldehyde as the active ingredient. Interest has been intense throughout the years for glutaraldehyde, right up to the present, as it still is essentially the gold-standard for chemical forms of sterilization. All disinfectants and new alternative disinfectant chemicals efficacy are based upon comparison to glutaraldehyde efficacy.

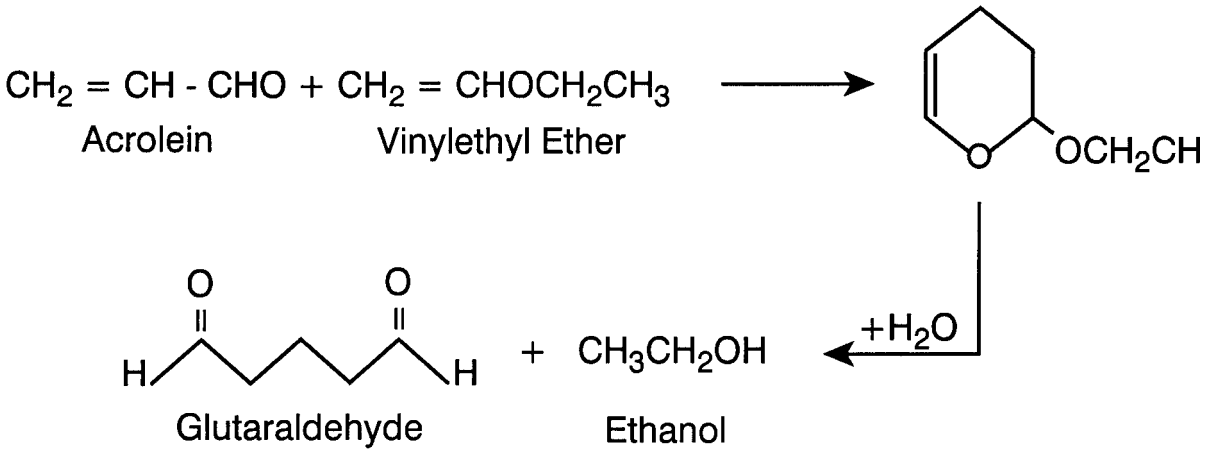


Figure 8

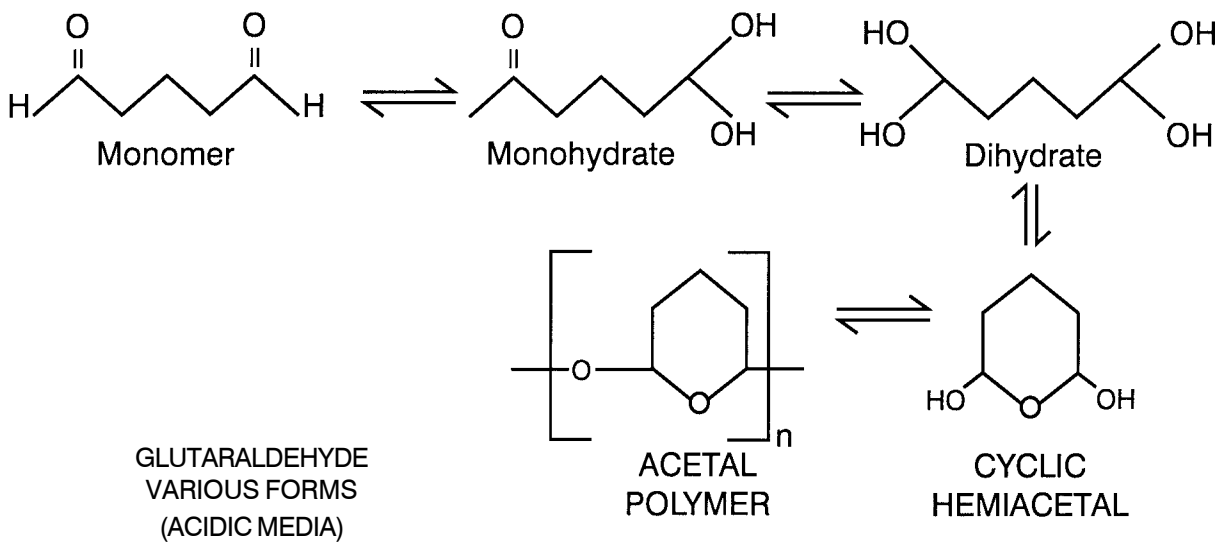
Glutaraldehyde rapidly was accepted and preferred in electron microscopy and pathology/histology labs as a superior alternative to formaldehyde. Tissue sections showed less distortion, brittleness, shrinkage, more total fixation on concentration/time frames and maintained elasticity during manipulation and sectioning, in addition to having longer shelf life. Glutaraldehyde was introduced into the embalming industry, essentially, by the Champion Company in the early 1960's through several patented formulations of glutaraldehyde and glutaraldehyde/formaldehyde based arterial, cavity and accessory chemicals.

Glutaraldehyde has also achieved high levels of acceptance and preferred use in the leather and hide tanning industry. Glutaraldehyde is the preferred aldehyde-based tanning chemical in the United States, virtually replacing formaldehyde, the older chemical standard. Glutaraldehyde tanned hides and leath-

ers exhibit better elasticities, less evidence of brittleness and cracking with wear, more suppleness and extended life, all of which creates higher levels of consumer acceptance.

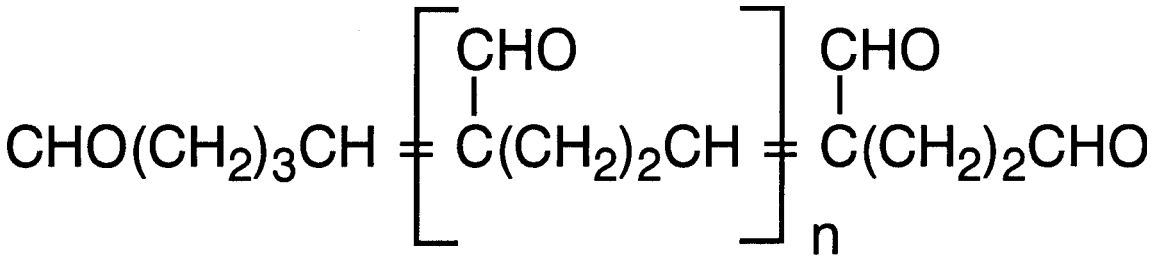
Commercially, glutaraldehyde is typically available in 2%, 25% and 50% solutions in water, with other dilutions occasionally seen and used. In acidic media, which is typically how glutaraldehyde is supplied to users, glutaraldehyde, being a highly reactive aldehyde, exists as a mixture of hydrated and non-hydrated forms. Therefore, monomer, open-chain mono-hydrates and di-hydrates, a cyclic hemiacetal and an acetal polymeric form all exist in a complex equilibrium. In acidic conditions, the cyclic hemiacetal and the acetal polymers of varying chain length are the preferred form and predominant (Fig. 9).

In neutral to basic media, this is not the case as glutaraldehyde spontaneously undergoes a self aldol-condensation reaction and dehydration to form α, β-unsaturated aldehyde polymers of varying chain length (Fig. 10). Effects of pH on reactivity demonstrate a steady increase of activity from pH4 to pH9, with maximum reactivity around pH of 8 or so. Above a pH9 there is a general decline in reactivity to pH11, after which little reaction capability is noticed. Precipitation type polymers are not common but can occur. Heated solutions demonstrate trimers, pentamers and heptamers with a trioxane skeleton and paraglut has been characterized as being 2, 4, 6-tris (4-oxobutyl)-1, 3, 5-trioxane, the polymeric form responsible for the white precipitate sometimes seen in stored glutaraldehyde solutions (Fig. 11).



GLUTARALDEHYDE
VARIOUS FORMS
(ACIDIC MEDIA)
Figure 9

In reaction with proteins the aldol polymers of glutaraldehyde react to form α, β-unsaturated imino type reaction products that are highly resonance-stabilized and very resistant to acid hydrolysis and rehydration (Fig. 12). Schiff base type reaction products that would be susceptible to acid hydrolysis and rehydration apparently do not form or survive during reaction. Epsilon-amino groups, (e.g. lysines) are particularly reactive and sterically accessible to glutaraldehyde. In addition, lysine residue analysis show pKa values of 8-8.5 (noted as a slight acid shift in the alkaline titration range) which seems to confirm the formation of michael-type adducts of aldol polymers that are acid-hydrolysis resistant. Schiff base type adducts would show pKa's of less than 5 to 6 and demonstrate susceptibility to rehydration, which is not the case with glutaraldehyde protein fixation. Another proposed bridged reaction product is a 1, 3, 4, 5-substituted pyridinium salt, similar to desmosine, an amino acid (Fig. 13).

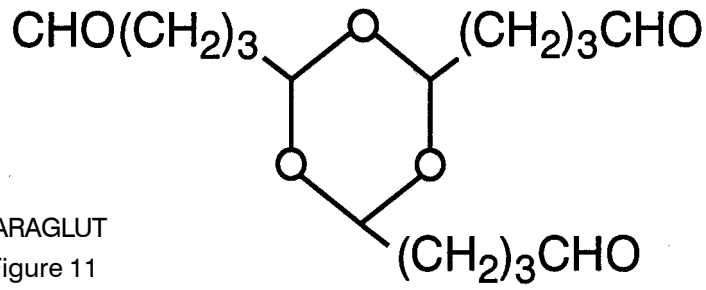


GLUTARALDEHYDE
ALDOL - TYPE POLYMER
Figure 10

From studies in the tanning industry, where acidic glutaraldehyde is the standard, effective fixation and cross-linking obviously occurs without a preponderance of unsaturated aldol-type reactants, indicating that bridging and cross-linking effectively occurs with unsaturation in acidic conditions.

In reaction, glutaraldehyde forms amino-methylols and then furthur condenses with other groups, such as phenolics, imidazoles, indoles, sulfhydryl of cysteine and to form bridged linkages. Very reactive sites appear to be terminal amine groups, α-amino groups of amino acid peptides, cysteine (via the -SH terminus), while imidazoles appear reactive but less preferred. Studies verifying high reactivity show 90% of free amino groups were reacted in 2 hours at pH6-7 with glutaraldehyde, while only 70% were reacted in formaldehyde at 7 days at a temperature of 35 degrees C. Cross-linking of proteins also occurs to a significant degree with studies of ovalbumin/bovine serum albumin aggregation showing 88% effectiveness in cross-linking.

In electron microsopy, OsO4 (osmium tetroxide) was the preferred fixation agent prior to the advent of glutaraldehyde. Glutaraldehyde was rapidly accepted as a superior fixative in this specialized field. Studies confirmed extremely fast reaction rates for glutaraldehyde (measured in minutes and hours) in contrast to formaldehyde which required days for complete endpoint fixation. Residual active - CHO (aldehyde) groups were found to be numerous after fixation and must be neutralized before processing into sections. This abundance of residual aldehyde moietites explains the time delayed fixation effects noticeable in glutaraldehyde treated tissues. Penetration and diffusion rates for glutaraldehyde are very slow with typical values of 2-3+mm of penetration on rat brain overnite. This is in sharp contrast to formaldehyde, which exhibits fast penetration/diffusion rates but very slow endpoint fixation rates. In fact, glutaraldehyde/formaldehyde mixtures are being employed as an effective fixative that combines the best attributes of both aldehydes. Glutaraldehyde reaction with lipids and nucleic acids is as expected based on aldehyde chemistry and is similar to that of formaldehyde.

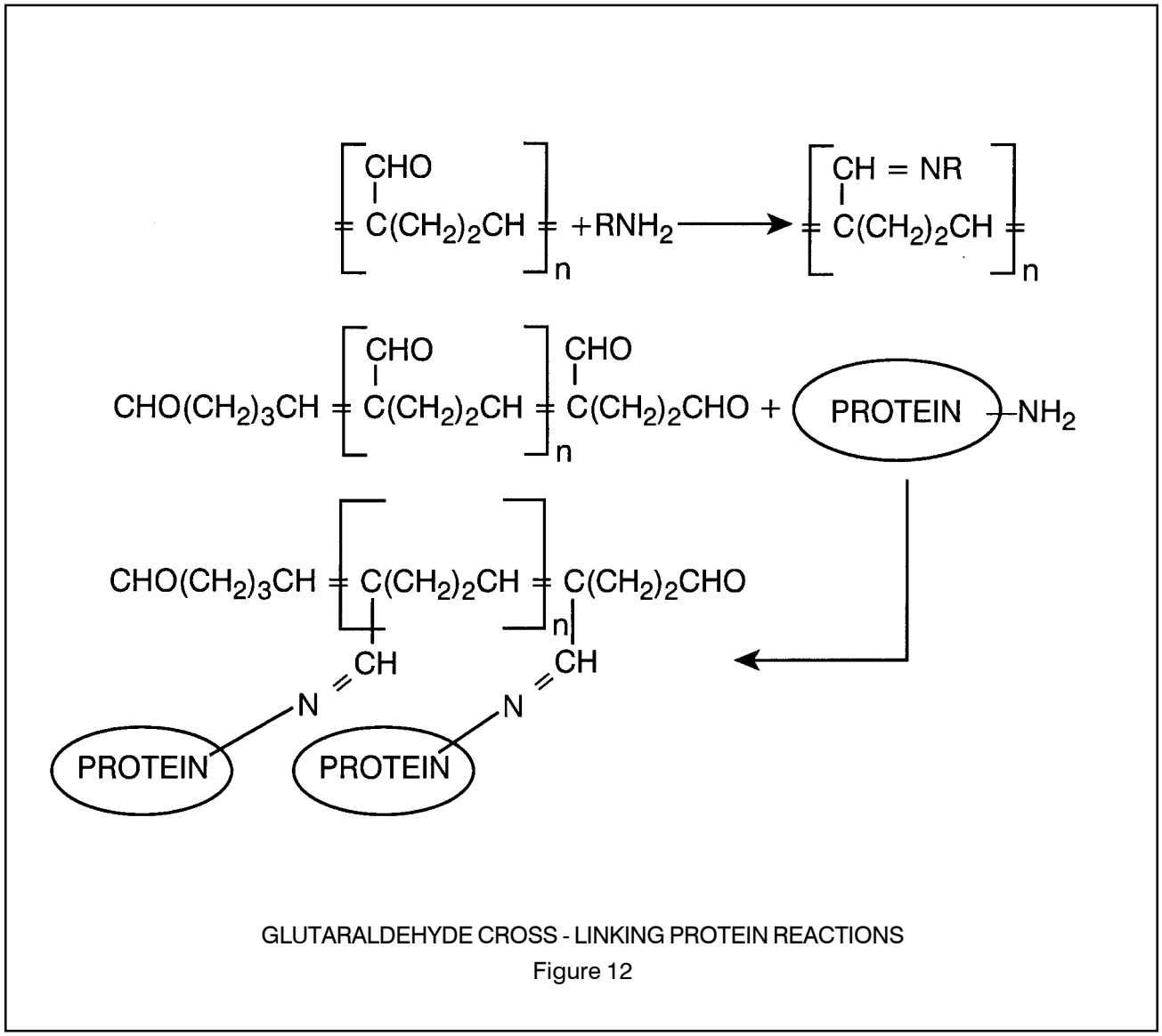


PARAGLUT
Figure 11

DISINFECTION/STERILIZATION: Formaldehyde is classified as a good high-level disinfectant and under most circumstances of use sporicidal as well. Effective concentrations range from a minimum accepted of 5% to typically 8% for consistent high-level disinfection/sterilization with time frames of action from a minimum of 3 hours to typically 8+ hours. Formaldehyde has been used for years in these disinfection scenarios with good results. Formaldehyde is a proven consistent and effective disinfectant in almost all clinical and industrial settings.

With the introduction of glutaraldehyde to the medical field, in the early 1960's, formaldehydes' popularity and usage has declined to very low levels (barely 5% of the total medical aldehyde disinfection/sterilant market). Almost no one markets a formaldehyde medical sterilant anymore in the U.S. Formaldehyde usage is more common in Europe, but still at fractional levels of what glutaraldehyde and alternatives are used at. Gigasept is a formaldehyde containing disinfectant that is used in Europe, but it has a helper aldehyde added for efficacy. Also popular in Europe, but seriously waning, is LTSF (low temperature steam formaldehyde) as disinfection/sterilization for heat-sensitive materials. Other

uses, still popular, are as a gas fumigant for biological safety cabinets and rooms, a gas bomb fumigant agent as a pesticide or disinfectant (generated usually by heating paraformaldehyde), and in poultry farms for incubators. Formaldehyde is also used as a general and effective, low-cost disinfectant and sanitizer for chicken coups, hog barns and dairy farms.

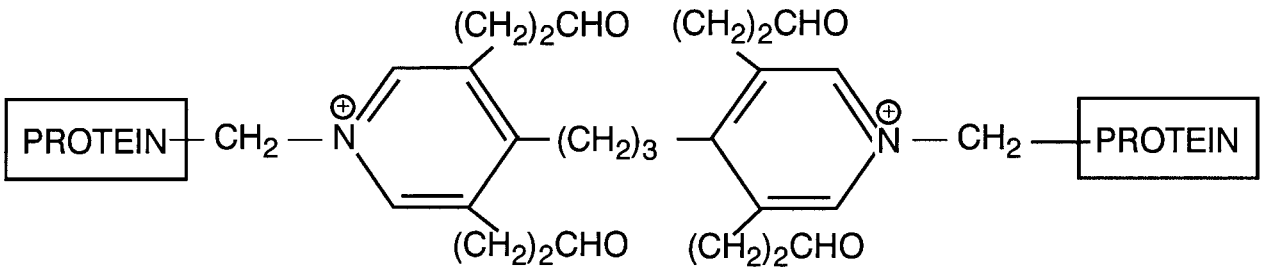


GLUTARALDEHYDE CROSS - LINKING PROTEIN REACTIONS

Figure 12

Glutaraldehyde is classified as an excellent high-level disinfectant/cold-chemical sterilant under almost all scenarios in which it is employed. Glutaraldehyde has, essentially, replaced formaldehyde as the premier aldehyde based disinfectant/sterilant. Glutaraldehyde is considered the gold standard to

which all other similar disinfectants/sterilants are compared. Glutaraldehyde consistently demonstrates efficacy at 2% concentrations for high-level disinfection and sterilization. Glutaraldehyde is superior to formaldehyde in both concentration and time factors—essentially demonstrating 2-4 times effectiveness at drastically reduced time exposures. Glutaraldehyde at 2% easily equilibrates to classical formaldehyde solutions of 5-8% and with equal or reduced contact times and capability of organic debris loading. Some modern glutaraldehydes are available at higher concentrations (2.8 and 3.2%) for faster cycle times, higher debris load, longer solution life and certainty of efficacy. Heated solutions are now popular to reduce contact times and insure sterilization.



GLUTARALDEHYDE LINKED REACTANT
Figure 13

EMBALMING COMPARISONS: From the above discussion, it is obvious that glutaraldehyde and formaldehyde are reactive aldehydes with significant protein fixation capability and embalming action. Formaldehyde is a fast diffuser and gives a rapid but reversible reaction with proteins. Glutaraldehyde, on the other hand, is a slow diffuser but delivers a rapid and non-reversible final reaction with proteins. Therefore, glutaraldehyde is expected to deliver more endpoint permanent fixation but perfuse the tissues slowly, while formaldehyde perfuses tissues rapidly but only forms irreversible fixation at a very slow rate. These facts result in very definite advantages and disadvantages of the respective aldehydes as embalming agents of human cadavers.

There are definite advantages in the use of formaldehyde for embalming. A rapid perfusion occurs which results in a fairly quick and noticeable coarse protein coagulation with early tissue firmness, which is easily observed by the embalmer. In conjunction with this rapid coagulation is a considerable dehydration reaction, mostly reversible but slowly converting to irreversibility over time. Dehydration is also encouraged by the natural wash-out of unreacted formaldehyde from tissues, which could be described as a type of secondary dilution. Formaldehyde, therefore is a very effective embalming agent

where fast reaction and dehydration ability is important, as in the case of edematous bodies.

Formaldehyde, unfortunately, has many drawbacks which weigh against its notable fast initial reactivity and ability to overcome edema. Actually, the rapid diffusion of formaldehyde and early reaction, that so impresses embalmers, is the cause of serious embalming problems. Too fast of a reaction results in the formaldehyde walling-off effect, formaldehyde burn, the wash-out effect and tissue shrinkage in non-edematous bodies. The result of high reactivity and rapid diffusion, therefore, hinders rathers than helps the overall embalming with sometimes disasterous effects. Bodies become very effectively superficially or shell-embalmed, but perfusion to underlying and deeper tissues is impeded or eliminated, resulting in a serious embalming problem 48-72 hours later. Everybody has embalmed a body with high index fluid to rock hardness that later, inexplicably, softens and shows classic signs of decomposition. What's the explanation for this?—rapid superficial embalming with little or no deep tissue perfusion and fixation which reverses and proceeds to a decomposition state.

Another major drawback is formaldehyde's inability to effectively embalm in a highly alkaline pH range. Many bodies currently encountered in embalming are saturated with nitrogenous byproducts of various disease states (e.g.-renal/hepatic failure, jaundice, pancreatic cancers, cancers in general, chemotherapy bodies, high titers of antibiotics and high blood levels of numerous therapeutics) in addition to being feeble and debilitated. Formaldehyde is at a serious disadvantage, in these situations, and sometimes extraordinary quantities of formaldehyde embalming agents are necessary to overcome this neutralization and inactivation effect.

The rapid reaction of formaldehyde also results in problems with clearing of blood-engorged tissues. The blood gravelling effect of formaldehyde is significant, and unless controlled and buffered, will result in poor clearing of superficial tissues during embalming with resultant staining evident. Ashen-greying is another serious unavoidable problem with formaldehyde embalming. Unless concealed by dyes or cosmetics, formaldehyde embalmed tissues exhibit a very unappealing death pallor, best described as putty-grey. This coloration is notorious in conjunction with formaldehyde embalming with poorly formulated, high index fluids with ineffective buffering and control agents.

Glutaraldehyde has many advantages to offer in embalming, the most important being relative imperviousness of reaction rate to pH changes, particularly in the alkaline range. Glutaraldehyde will react with protein at higher pHs that would essentially render formaldehyde inactive. Because of slow diffusion/perfusion rates, reaction with blood and blood-perfused tissues is slow with minimum initial coagulation. Clearing of blood from tissues is, therefore, strongly enhanced relative to formaldehyde.

There is minimal or no walling-off effect, tissue burning reaction or superficial rapid embalming as would be typical with formaldehyde. Cosmetic effects of embalming is noticeably better than with formaldehyde, with no greying or ashen-whitening effect noticeable. Tissues overembalmed with glutaraldehyde will show a yellowish-tanning coloration and severe overembalming will significantly darken tissues. Fortunately, these effects are easily overcome, in most instances, with tissue dyes during injection. A very important advantage of glutaraldehyde over formaldehyde is in regards to sanita-

tion potential. Ounce for ounce, glutaraldehyde, through its superior disinfection/sterilization capabilities, which are well documented in the medical field, is far more effective as a sanitizing agent in embalming than formaldehyde. Formaldehyde can only equal this sanitizing ability by the use of an overwhelming concentration, which is counterproductive to good embalming results.

The major disadvantage of glutaraldehyde in embalming is slow diffusion/perfusion rate. This results in most of the classical signs of embalming appearing very late or not at all to the embalmer during the embalming. The bodies will not stiffen and harden rapidly, if at all, dehydration and skin tightness will not be evident, and the bodies will usually display a lifelike appearance that, to the embalmer, belies the confirmation of embalming. In addition, the embalmed body will further firm and harden over time and possibly darken as delayed additional fixation occurs. This physical symptomology is opposite that noted in formaldehyde embalming, against all precepts taught in embalming training, and counter-intuitive to the average embalmer. Glutaraldehyde infused bodies appear nothing like traditional formaldehyde embalmed corpses. Invariably, rigidity is minimal, skin elasticity is extreme, dehydration is non-existent, lifelike appearance is typical, and flexibility is considerable. Most embalmers would interpret this set of observables as evidence of lack of embalming. Actually, it is no more than evidence of lack of sequelae of formaldehyde embalming and nothing more.

This leads us, inevitably, to the precepts of the formaldehyde-apology industry. Basically, the arguments are this: 1. there is nothing besides formaldehyde on the face of the earth that is usable by the funeral industry for the embalming of dead human bodies, 2. therefore, formaldehyde is not to be questioned or called to task for any reason (health effects, exposure dangers, embalming efficacy or otherwise), 3. Under all circumstances, formaldehyde is to be justified as safe and effective in the embalming industry, for to do otherwise is to stare into the abyss. The inevitable fallout of this paradigm is the accusation that glutaraldehyde does not embalm or fix tissues.

This is a difficult one to profess. Chemical aldehyde reactivity goes hand-in-hand with sanitizing/disinfecting/sterilizing ability, tanning/fixation ability and histology/pathology fixation. To profess that, yes, glutaraldehyde is a proven tanning chemical, yes, glutaraldehyde is a proven aldehyde disinfectant/sterilant, yes, glutaraldehyde is a proven histology/pathology fixative, but, alas, glutaraldehyde does not embalm tissue -- is patently absurd. This tack is understandable but untenable.

One example may serve to enlighten. I personally have embalmed approximately 1000 bodies with a certain chemical (JaunDial) which contains a mix of glutaraldehyde and formaldehyde with the usual buffers, penetrants and control chemicals characteristically found in modern embalming fluids. The percentage of formaldehyde present in JaunDial is barely 4.0%, which means in my 1000 embalmings of typically normal and jaundice bodies (some of which were held up to 2 weeks before interment), the amount of formaldehyde in the total embalming was approximately 3/4 ounce. Therefore, I am led to believe that the typical 175 pound human cadaver, which demonstrated excellent preservation and cosmetic effect, in almost all cases, was solely due to the influence of 3/4 ounce of formaldehyde?!

Anatomical cadavers and specimens have been infused with glutaraldehyde embalming fluids and remain preserved after years, viscera has been treated with Cavity 48, a glutaraldehyde-based cavity fluid with no formaldehyde, the body then buried and disinterred after a year with evidence of extreme mummification and petrification present. Countless glutaraldehyde infused and saturated specimens exist in labs across the globe after decades. Hundreds of tons of leather products exist that were fixed/tanned by glutaraldehyde—how is it possible that these preserved animal skins are candidates for decomposition after decades of use and wear? The documentary and evidentary list goes on and on. I will not belabor the point, but to say, that the accusation that glutaraldehyde does not embalm is untenable.

What is possible is a poorly embalmed body resulting from a poorly planned and executed embalming using a poorly formulated glutaraldehyde injection chemical—so what else is new?—this happens all the time in traditional formaldehyde embalming. Where do the decomposed bodies in disinterments, putrefaction in delayed burials, persistent skinslip, tissue gas cases, and all the miasmatic mausoleums come from? Virtually all can be traced to a traditional formaldehyde embalming. All preservatives/fixatives, aldehydes or otherwise, will fail under certain circumstances of use, due to a constellation of chemical inhibition, physical parameters of infusion, unwanted cross-reactions and bad luck. No embalming chemical is immune from these causes of poor embalming results.

SUMMARY AND CONCLUSION: Formaldehyde and glutaraldehyde each have much to offer to the modern embalming industry. Formaldehyde excels in certain embalming scenarios, such as edema, and presents rapid and classical results familiar to embalmers. Glutaraldehyde excels at sanitizing ability, mildness of reaction, tissue clearing, cosmetic effect and prolonged, delayed action. Glutaraldehyde is excellent in cavity fluids where contact times are long and resistant fixation is essential. In arterial injections of typically normal bodies, pre-injection of glutaraldehyde followed by formaldehyde injection to rapidly induce hardness of tissue, or injection of glutaraldehyde/low formaldehyde mixes, to moderate reaction, yield excellent results. It is shocking how little formaldehyde is needed to yield classical signs of embalming (firmness, rigidity, skin tightness) in normal body injections (typically 4-6 ounces in the last part of the injection of a moderate concentration [index 20] fluid). Injections that stress and take advantage of the inherent advantages of both aldehydes yield the consistently best embalming results. The overall goal of chemical selection mix in the modern embalming room should be a juxtaposition of lowered total overall exposure risk balanced against sufficient and effective embalming results, but that is a topic for another day.

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