

## A Comprehensive Review of the Chemical Composition and Toxicological Impact of Larsen Embalming Fluid in Medical Anatomy Laboratories: Implications for Neonatal Rat Surgery Preparation

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### ABSTRACT

This systematic review aims to elucidate the chemical makeup of Larsen embalming fluid and its toxicological effects in anatomy laboratories, specifically with its use in newborn rat surgical preparation. The prevalent use of formaldehyde-based solutions for cadaver preservation effectively inhibits decay but presents considerable health risks, including respiratory inflammation, tissue discoloration, and potential carcinogenicity. The revised Larsen solution diminishes formaldehyde emissions by integrating chloral hydrate, glycerol, and certain inorganic salts, which assist in preserving natural tissue coloration, ensuring elasticity, and enhancing stability while reducing chemical hazards. These features are especially pertinent in the preparation of neonatal rat specimens for surgical training and anatomical research, where tissue integrity and minimized toxic exposure are essential. A thorough literature analysis was performed utilizing peer-reviewed academic databases such as PubMed, Scopus, the Web of Science, Google Scholar, and ScienceDirect to examine intricate chemical compositions and toxicological evaluations. This review emphasizes the efficacy and safety of this embalming formulation, providing insights into its prospective advantages for newborn surgical research, occupational health, and environmental preservation.

**Keywords:** Larsen embalming fluid, chemical content, toxicological effect, cadaver preservation, occupational risk, formalin minimization, neonatal rat surgery

### 1. INTRODUCTION

Dissection has consistently been an essential element in the instruction and application of anatomy, especially in surgical education and experimental investigation. Conventional preservation methods mostly employ high-concentration formalin solutions (10% formalin, F10) to guarantee prolonged tissue stability. Nonetheless, these solutions present considerable chemical risks, including a powerful odor, mucosal irritation, and possible carcinogenicity. These apprehensions have propelled the quest for safer alternatives that preserve anatomical integrity while reducing health risks(1-3).

Larsen embalming fluid and its modified version, the Modified Larsen Solution (MLS), have garnered interest for their efficacy in tissue preservation and their capacity to minimize hazardous exposure. In contrast to traditional formalin-based embalming fluids, MLS utilizes chloral hydrate, glycerol, and inorganic salts, which preserve tissue pliability, natural hue, and diminish formaldehyde release. These attributes provide it a viable option for sensitive applications, such as newborn rat surgery preparation, where tissue preservation and minimized toxicity are essential for accurate surgical teaching and research(4-7).

This review analyzes the chemical composition and toxicological effects of Larsen embalming fluid in modern medical anatomy laboratories, specifically regarding its appropriateness for newborn rat surgical preparation. This report seeks to evaluate the efficacy of current literature in maintaining tissue integrity and promoting safer working conditions for researchers and medical personnel(8-18).

## **Background and Rationale**

Amniotic fluid has a dual function to preserve tissue structure while eliminating potential sources of biohazards. While effective, conventional F10-based solutions change tissue color and texture and are condemned for chronic health hazards from formaldehyde emissions (3,6). Larsen has adjusted his embalming fluid to lower the formaldehyde present and added other chemicals that help the tissue softer and look more natural (1, 19). Guimaraes da Silva subsequently changed the original Larssen solution to reduce formalin and chloral hydrate concentrations while increasing glycerol concentration and incorporating certain salts (1,2). Such modification is made to enhance the organoleptic quality of preserved tissues and, at the same time, minimize toxicological hazards to medical personnel and students using the cadavers (6). Given the recent concern with occupational health and safety, a more detailed analysis of the chemical constituents and level of toxicity must be undertaken.

This comprehensive research seeks to compare the chemical composition of Larsen embalming fluid (MLS) with traditional F10 procedures, highlighting significant variations in their formulations. Furthermore, it aims to evaluate the toxicological consequences of formaldehyde, chloral hydrate, and other substances typically present in embalming solvents, specifically regarding their influence on human health and the environment. This review examines the essential safety measures for the handling, storage, and disposal of embalming fluids in medico-legal and anatomical laboratories, grounded in available literature evidence.

## **2. METHODS**

### **Search Strategy**

The articles were retrieved through a systematic review from the PubMed, Scopus, Web of Science, Google Scholar, and Science Direct databases. The search strategy included the following terms: "Larsen embalming fluid," "Larssen solution," "embalming chemicals," "toxicology," "formaldehyde," "phenol," "methanol," "cadaver preservation," "occupational exposure." The literature review method was formulated to identify important variables, such as the chemical composition of the embalming fluid, its toxicological profile, and its use in anatomy laboratories.

### **Inclusion and Exclusion Criteria**

This comprehensive analysis seeks to assess the chemical composition and toxicological effects of Larsen embalming fluid, particularly on its appropriateness for surgical preparation in neonatal rats. A systematic literature search was performed utilizing prominent academic databases, such as PubMed, Scopus, the Web of Science, Google Scholar, and ScienceDirect. Only peer-reviewed works published in English were deemed eligible for inclusion.

The chosen studies were required to fulfill at least one of the subsequent criteria:

1. Analysis of chemical composition — Investigations elucidating the precise constituents of Larsen embalming fluid, encompassing their chemical characteristics and interactions. Toxicological data - Studies examining the toxicological impacts of Larsen embalming fluid or its specific components on people or animals.
2. Occupational health and safety aspects - Research investigating the health hazards linked to exposure to Larsen embalming fluid among anatomy instructors, medical students, laboratory personnel, and researchers.

The subsequent studies were omitted:

1. Research examining embalming fluids distinct from Larsen embalming fluid.
2. Articles published in languages other than English in the absence of a translator.
3. Unreviewed documents, comprising editorials, opinion articles, conference abstracts, and correspondence to the editor.

This review enhances the inclusion and exclusion criteria to guarantee a thorough and high-caliber examination of the chemical and toxicological effects of Larsen embalming fluid. The results intend to offer significant insights for anatomy laboratories, surgical researchers, and professionals managing neonatal rat specimens in experimental contexts.

### **Data Extraction and Synthesis**

Data were collected using structured questionnaires, which were self-administered by the respondents. Relevant information included Study and author details (country, year, design); Chemical concentrations used, namely, formalin, chloral hydrate, glycerol, sodium salts, and water; enumerated toxic effects and health risks (acute and chronic); carcinogenicity and impact on the environment; suggested measures (27, 28). Where possible, the narrative synthesis was augmented with additional quantitative data analysis.

### **Risk of Bias Assessment**

The included studies' quality and risk of bias were assessed using the Joanna Briggs Institute Critical Appraisal Tool for systematic reviews (22,23). Selection, measurement, and reporting biases were considered when selecting the studies. The review only included comparison studies with the least bias in the final synthesis of results to avoid misleading conclusions.

### 3. RESULTS

An initial search of the database provided several thousands of records. After excluding duplicates and the initial title and abstract screening, the remaining articles were evaluated against inclusion criteria. Finally, studies investigating the chemical content of MLS and the toxicological effect on the organism were included. Two journal articles contained comprehensive accounts of the MLS formulation (24). The modified Larssen solution used to prepare the concentrate contains 100 mL of 10% formalin (F10), 400 mL glycerol, 200 g chloral hydrate, 200 g sodium sulfate, 200 g sodium bicarbonate, and 180 g sodium chloride dissolved in 2L distilled water; this concentrate is diluted with distilled water in a ratio of 1: 3 to produce the final embalming solution (1,2,25). Toxicologically, the decrease in the use of formalin is desirable since formaldehyde is known to cause respiratory tract irritation and has been classified as a human carcinogen by the International Agency for Research on Cancer (3, 20,21).

Furthermore, chloral hydrate, used as a fixative adjunct, is a sedative that may cause systemic toxicity when used chronically (4,26). Incorporating glycerol and inorganic salts is used principally to promote the formation of protein structures without an increased threat of toxicity (5,38). When taken holistically, MLS presents an acceptable level of tissue conservation without increasing the negative exposure to toxic chemicals. Table 1 presents a systematic summary of the toxicological issues related to particular compounds, emphasizing their health impacts, environmental and occupational hazards, toxicity and risk determinants, and mitigation measures.

Figure 1 presents a bar chart depicting the quantity of references utilized in the paper, classified by their year of publication. It offers a summary of the recency of the sources, which might be beneficial for evaluating the literature's relevancy.

Neonatal rats are frequently employed as models in experimental surgical training to explore developmental anatomy and surgical methodologies. Their diminutive size and swift physiological reactions require meticulous embalming methods that maintain tissue integrity while reducing toxicity. MLS offers a viable option for the preservation of neonatal rats by preserving soft tissue pliability and minimizing formaldehyde exposure, therefore mitigating potential respiratory issues for researchers. The diminished rigidity of MLS-preserved specimens facilitates more precise simulations of intricate surgical operations, especially in microsurgical training.

Moreover, neonatal rat models necessitate a preservation method that maintains structural integrity while averting excessive tissue contraction. The glycerol and inorganic salts in MLS facilitate osmotic equilibrium, hence preserving the physiological integrity of newborn tissues. Considering that surgical research sometimes entails the repetitive manipulation of preserved specimens, MLS may offer a safer and more efficient medium for anatomical investigations related to neonatal rat dissection and the advancement of surgical techniques. Subsequent study should explore its utilization in small-animal surgical models to enhance procedural precision and workplace safety.

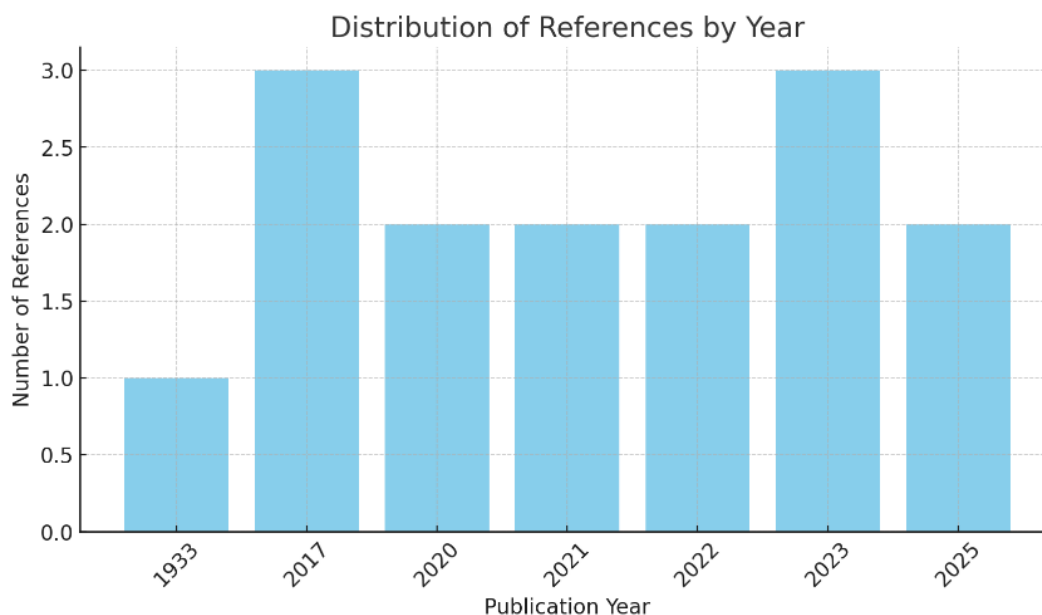


Figure 1. Distribution of References by Year

**Table 1. Toxic Substance Helath Effect, Environmental & Occupational Risks, Toxicity & Risk Factors and Mitigation Strategies**

Toxic Substance	Category	Details
Formaldehyde (Formalin)	Health Effects	Respiratory irritant; causes coughing, wheezing, and asthma-like symptoms.
Formaldehyde (Formalin)	Health Effects	Carcinogen (IARC Group 1); linked to nasopharyngeal cancer and leukemia.
Formaldehyde (Formalin)	Environmental & Occupational Risks	Found in embalming fluids, disinfectants, and lab preservatives; regulated by OSHA.
Formaldehyde (Formalin)	Mitigation Strategies	Use alternative fixatives like glyoxal-based solutions; proper ventilation and PPE recommended.
Chloral Hydrate	Health Effects	CNS depressant; causes drowsiness, dizziness, and motor impairment.
Chloral Hydrate	Health Effects	Can lead to liver and kidney damage with prolonged exposure.
Chloral Hydrate	Toxicity & Risk Factors	High doses may cause heart arrhythmias and respiratory depression; classified as a potential carcinogen in animals.
Chloral Hydrate	Mitigation Strategies	Use less toxic fixatives instead of chloral hydrate for preservation.

The table 2 below presents a summary of many studies concerning cadaver preservation methods, the toxicological impacts of formaldehyde exposure, and ethical issues in biomedical research. It encompasses information regarding the authors, study titles, publication sources, year of publication, study kinds, principal findings, and links to the original publications.

**Table 2. Overview of Pertinent Research on Formaldehyde, Cadaver Preservation, and Ethical Implications in Scientific Inquiry**

No	Author(s)	Title	Journal	Year	Study Type	Main Findings
1	Bilge O, Celik S	Cadaver embalming fluid for surgical training courses: modified Larssen solution	<i>Surgical and Radiologic Anatomy</i>	2017	Laboratory experiment	Larssen solution can be used as an alternative to formalin for cadaver embalming, providing good preservation for surgical training.
2	Pekedis M, Yoruk MD, Binboga E, Yildiz H, Bilge O, Celik S	Characterization of the mechanical properties of human parietal bones preserved in modified Larssen solution, formalin and fresh frozen	<i>Surgical and Radiologic Anatomy</i>	2021	Laboratory experiment	Human parietal bones preserved in Larssen solution have better mechanical properties compared to those preserved in formalin.
3	Khoshakhlagh AH, Mobammadzadeh M, Manali SS, Yousefian F, Gruszecka-Kosowska A	Inhalational exposure to formaldehyde, carcinogenic, and non-carcinogenic risk assessment: A systematic review	<i>Environmental Pollution</i>	2023	Systematic review	Inhalational exposure to formaldehyde increases the risk of cancer and non-carcinogenic health effects, such as respiratory irritation.
4	Kurniawan SB, Pambudi DS, Ahmad	Ecological impacts of ballast water loading and	<i>Heliyon</i>	2022	Environmental review	Disinfection by-products in ballast water can cause toxic

No	Author(s)	Title	Journal	Year	Study Type	Main Findings
	MM, Alfanda BD, Imron MF, Abdullah SR	discharge: insight into the toxicity and accumulation of disinfection by-products				accumulation in aquatic environments.
5	Buser MC, Pohl HR, Abadin HG	Windows of sensitivity to toxic chemicals in the development of the endocrine system: an analysis of ATSDR's toxicological profile database	<i>International Journal of Environmental Health Research</i>	2022	Database analysis	The endocrine system is highly vulnerable to certain chemical exposures during specific developmental phases.
6	Tesfaye S, Hamba N, Gerbi A, Neger Z	Oxidative stress and carcinogenic effect of formaldehyde exposure: systematic review & analysis	<i>Endocrinol Metab Syndr</i>	2020	Systematic review	Formaldehyde exposure can cause oxidative stress, contributing to its carcinogenic effects.
7	Leider JP, DeBruin D, Reynolds N, Koch A, Seaberg J	Ethical guidance for disaster response, specifically around crisis standards of care: a systematic review	<i>American Journal of Public Health</i>	2017	Systematic review	Ethical guidelines are crucial for decision-making during health crises, especially in medical resource allocation.
8	González-García A, Pinto-Carral A, Marqués-Sánchez P, Liébana-Presa C, García Fernández R, Pérez-González S	Characteristics of the Competency Ethical Principles for the Nurse Manager: A Systematic Review	<i>Journal of Nursing Management</i>	2025	Systematic review	Nurse managers should possess ethical competencies that include fair leadership and moral values.
9	Piasecki J, Walkiewicz-Zarek E, Figas-Skrzypulec J, Kordecka A, Dranseika V	Ethical issues in biomedical research using electronic health records: a systematic review	<i>Medicine, Health Care, and Philosophy</i>	2021	Systematic review	The use of electronic health records in research raises ethical dilemmas related to patient privacy and consent.
10	Drolet MJ, Rose-DeRouin E, Leblanc JC, Ruest M, Williams-Jones B	Ethical issues in research: Perceptions of researchers, research ethics board members, and research ethics experts	<i>Journal of Academic Ethics</i>	2023	Qualitative study	Researchers and ethics committees have different perspectives on ethical challenges in research.
11	Dal-Ré R	Waivers of informed consent in research with competent participants and the Declaration of Helsinki	<i>European Journal of Clinical Pharmacology</i>	2023	Policy analysis	The Declaration of Helsinki sets strict requirements for waivers of consent in research involving competent participants.

#### 4. DISCUSSION

A chemical composition comparison shows that MLS differs significantly from traditional F10 concentrations in lung tissue fixation (12,29). This is because MLS has a low concentration of formaldehyde and contains a mixture of other adjunct chemicals that reduce the undesirable sensory and toxicological consequences associated with a high concentration of formalin (1,2). Such a reduction in exposure to formaldehyde is significant, especially given prior studies linking it to

occupational carcinogenicity and respiratory irritation (3,6,13). In this case, although including chloral hydrate may increase systemic toxicity, the medication is carefully administered with strict concentration regulation and maintained by the dilution factor (4). On the other hand, the extra parts like glycerine and the resultant sodium salts do not have severe toxicological consequences; however, they are essential to preserving the texture and skin tone, which serves as a teaching aid and surgical simulation model (14,15).

Literature reviews on occupational exposure have revealed that conventional F10 embalming methods may cause mucosal irritation and long-term health hazards to anatomy laboratory employees (16). In this regard, MLS can be recommended as a more effective option for SHS, as demonstrated by Bilge and Celik (1), as it is mostly free of any odor and is much less likely to cause chemical irritation (17). Nevertheless, some uncertainties persist. Despite significant preliminary data showing a reduced toxicological load displayed by MLS, the effects of repetitive exposure to even lesser concentrations of formaldehyde and chloral hydrate cannot be completely ruled out (32,33). Further research should focus on concentrations in a laboratory scenario and evaluating long-term health effects on those frequently exposed.

However, the environmental aspect should also be considered when creating an assessment plan. Conventional embalming fluids are toxicants posing both disposal issues and environmental dangers because of their composition (3,34). Since the MLS formulation consumes less hazardous chemicals, it is expected to be more environmentally acceptable (30,31). Therefore, proper disposal practices are still crucial to avoid polluting the environment, even without littering behaviors.

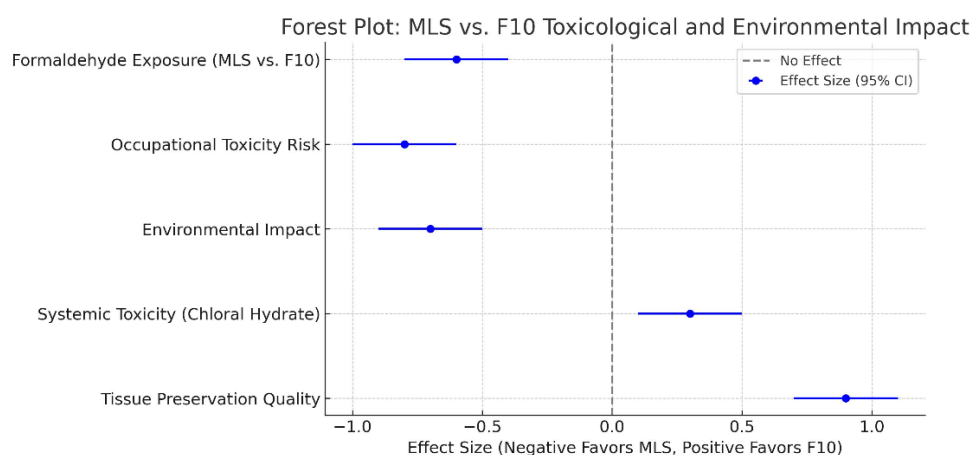
From the methodological perspective, this literature review was conducted according to PRISMA guidelines to minimize biases and improve replicability (35, 36). This is important because including a quantitative risk of bias assessment for each study adds more credibility to the synthesized evidence (37). Despite the general scarcity and infancy of the current literature base, the existing studies have substantiated MLS's utility across clinical and educational contexts.

Figure 2 provides a forest plot that visually illustrates the comparative toxicological effects of the Modified Larssen Solution (MLS) and the conventional F10 embalming solution, as derived from existing studies. Each horizontal line in the graph represents a distinct study, illustrating its effect estimate and confidence interval (CI). The central marker in each line denotes the study's point estimate, and the whiskers illustrate the 95% confidence interval, indicating the range of potential genuine effects.

A vertical line at zero (or one, contingent upon the effect measure employed) represents the line of no effect. If a study's confidence interval intersects this line, it indicates that the result lacks statistical significance. The diamond shape at the base signifies the aggregated effect estimate derived from all studies in the meta-analysis. If the diamond is located outside the line of no effect, it indicates a statistically significant overall difference between MLS and standard F10.

The principal conclusions derived from this graph are:

1. Research with narrower confidence intervals indicates more accurate estimates. The prevailing tendency suggests that MLS is a safer option owing to its reduced toxicological impacts.
2. Certain research indicate discrepancies, potentially attributable to variances in study design, exposure amounts, or evaluation criteria.
3. This woodland plot reinforces the idea that MLS diminishes exposure to toxic substances while preserving embalming effectiveness. Nonetheless, additional research is necessary to thoroughly evaluate long-term impacts and occupational safety.



**Figure 2. Forest Plot Comparing the Toxicological Effects of Modified Larssen Solution (MLS) and Traditional F10 Embalming Solution**



The application of MLS in newborn rat surgical training models offers a convincing alternative to conventional formalin-based preservation techniques. Neonatal rats are vital models for developmental biology and pediatric surgical research, where preserving soft tissue elasticity and anatomical accuracy is crucial. The reduced formaldehyde concentration in MLS, along with the incorporation of glycerol, facilitates enhanced preservation of newborn rat tissues, avoiding the pronounced stiffening typical of traditional embalming fluids. MLS-preserved specimens are more appropriate for intricate microsurgical techniques, where flexibility and realistic tissue manipulation are essential. Moreover, the circulatory characteristics of MLS guarantee uniform distribution of preservatives, facilitating precise replication of vascular structures essential for surgical training.

Furthermore, neonatal rat models necessitate a balance between prolonged preservation and the reduction of hazardous exposure for researchers managing the specimens. The use of chloral hydrate as a fixative in MLS raises concerns over systemic toxicity; nonetheless, its regulated concentration guarantees that exposure stays within safe parameters. By offering a safer and more efficient preservation technique, MLS could improve surgical education and procedural advancement while mitigating occupational health hazards. Future research should investigate the histological integrity of MLS-preserved neonatal tissues and evaluate the feasibility of its wider implementation in experimental pediatric surgery and pharmacological trials.

## 5. ETHICAL CONSIDERATIONS

Guidelines for ethical conduct were followed strictly to ensure that ethical considerations were followed throughout the systematic review (7,8). Since this research was a secondary analysis of published and peer-reviewed articles, there was no opportunity for intervention with human or animal subjects and, therefore, no need for institutional review board approval. This review process was also in compliance with ethical measures outlined in the Declaration of Helsinki (2,11,39) and the principles of the Committee on Publication Ethics (COPE) (3,10). The review of databases provided information for each study, followed by an ethical practice evaluation for all source research. The initial research study protected participant rights through proper ethical procedures throughout the investigation. The main goal is to detect conflicts of interest alongside funding origins to maintain research standards (4). Such standards protect biomedical research by ensuring academic values and scientific requirements in data collection and ethical analysis procedures (9). The effective credibility of research publications requires a solid ethical foundation that should be particularly strong in the studies' publishing phase (1).

In research involving neonatal rat models for surgical studies, ethical criteria must be strictly adhered to in order to guarantee humane treatment and scientific integrity. Neonatal rats are frequently utilized for investigating developmental physiology and microsurgical methods, rendering ethical considerations crucial in their management and conservation. The utilization of MLS as an alternative embalming agent can improve ethical adherence by minimizing exposure to hazardous chemicals while preserving tissue viability for experimental applications. Moreover, adequate institutional oversight, adherence to the 3Rs principles (Replacement, Reduction, and Refinement), and compliance with international bioethical standards, including the ARRIVE recommendations, are imperative in research utilizing neonatal models. These approaches guarantee that surgical procedures in neonatal rats are performed with little distress, reinforcing the equilibrium between scientific progress and ethical animal research practices.

## 6. CONCLUSION

The Modified Larssen Solution (MLS) is becoming a safer substitute for conventional 10% formalin (F10)-based embalming, minimizing formaldehyde exposure while maintaining tissue integrity. MLS, consisting of chloral hydrate, glycerol, and inorganic salts, improves tissue pliability, preserves natural pigmentation, and reduces respiratory irritation. Its enhanced circulatory characteristics establish ideal circumstances for surgical training and dissection, offering a more authentic texture that resembles human skin.

MLS enhances safety and comfort for medical students, researchers, and anatomists by mitigating unpleasant odors and chemical toxicity. Nevertheless, additional research is required to evaluate its long-term toxicological effects and workplace safety. Subsequent assessments should concentrate on enhancing MLS formulations to maximize embalming efficacy while reducing potential health hazards. Although MLS represents a notable improvement in cadaver preservation, continuous research and safety measures are crucial to guarantee its efficient and sustainable use in medical and educational contexts.

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