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The Role of Pharmacists in Preventing Complications Associated with Intravenous Medication Incompatibilities

Ahmed Mohammad Husien Mahdi[1], Saeed Abdullah Alzhrani[2], Abdulkrim Hamoud Ayed Alzabni[3], Omar Moidh Alsukhayri[4], Meshal Abdulaziz A Alharbi[5], Alzabni Faihan Obaid H[6], Alsliem, Khaleed Abdulkarem A[7], Faris Saad H Alruwaili[8], Mohammed Ibrahim Inad Alwushayh[9], Alwushayh, Ashraf Abdullah M[10]

[1] Pharmacy Technician — Mental Health Hospital – Jeddah First Health Cluster – Ministry of Health – Jeddah – Makkah Region – Saudi Arabia.
Email: ahmad2323@windowslive.com
[2] Pharmacist — Mental Health Hospital – Jeddah First Health Cluster – Ministry of Health – Jeddah – Makkah Region – Saudi Arabia. Email: saalzhrani@moh.gov.sa
[3] Pharmacy — King Salman Specialist Hospital – Hail Health Cluster – Ministry of Health – Hail – Hail Region – Saudi Arabia. Email: aarashedi2920@gmail.com
[4] Pharmacy Technician — Children's Hospital – Taif Health Cluster – Ministry of Health – Taif – Makkah Region – Saudi Arabia. Email: omr110010@gmail.com
[5] Pharmacy Technician — Nabhaniyah General Hospital – Qassim Health Cluster – Ministry of Health – Al-Nabhaniyah – Qassim Region – Saudi Arabia.
Email: malharbi399@moh.gov.sa
[6] Pharmacist — Branch of the Ministry of Health in Hail Region – Ministry of Health – Hail – Hail Region – Saudi Arabia. Email: faihan99@hotmail.com
[7] Pharmacy Technician — Prince Abdulaziz bin Musaed Hospital – Northern Borders Health Cluster – Ministry of Health – Arar – Northern Borders Region – Saudi Arabia.
Email: Khalody.333@hotmail.com
[8] Pharmacy Technician — King Abdulaziz Specialist Hospital – Al Jouf Health Cluster – Ministry of Health – Sakaka – Al Jouf Region – Saudi Arabia.
Email: fareis.saad@gmail.com
[9] Pharmacist — Dumat Al-Jandal General Hospital – Al Jouf Health Cluster – Ministry of Health – Dumat Al-Jandal – Al Jouf Region – Saudi Arabia. Email: Mom-9@msn.com
[10] Pharmacist — Al Jouf Health Cluster – Ministry of Health – Sakaka – Al Jouf Region – Saudi Arabia. Email: Aalwushayh@moh.gov.sa

ABSTRACT: Intravenous (IV) medication incompatibilities represent a persistent and clinically significant threat to patient safety across hospital settings, particularly in intensive care units where polypharmacy and limited vascular access converge. Physicochemical reactions between co-administered drugs can produce visible precipitates, subvisible particles, loss of therapeutic potency, catheter occlusion, embolic events, and systemic inflammatory responses, with reported incompatibility rates reaching 61.4% of critically ill patients and contributing to up to 25% of medication errors in critical care. Pharmacists occupy a uniquely strategic position to intercept these hazards at multiple points along the medication-use process, including prescription review, compatibility screening,

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compounding oversight, smart pump library management, and interdisciplinary education. Evidence demonstrates that pharmacist-led pre-issue compatibility monitoring achieves acceptance rates exceeding 90%, that clinical pharmacist participation in bedside rounds reduces incompatibility-related prescribing, and that pharmacy-driven smart pump compliance initiatives substantially improve drug library adherence. Nevertheless, persistent barriers—including incomplete compatibility databases, pharmacist workforce shortages, alert fatigue, and knowledge deficits among prescribers and nurses—limit the full realization of pharmacist potential in this domain.

INTRODUCTION

The administration of intravenous medications is an indispensable component of modern hospital care, yet it is also one of the most error-prone processes in the medication-use system [1]. Unlike other routes, the intravenous route bypasses natural absorptive and metabolic barriers and delivers drug directly into the systemic circulation with immediate and potentially irreversible consequences when something goes wrong [2]. Drug incompatibility occupies a central position among intravenous safety threats because it arises from the convergence of pharmacological properties, prescribing decisions, compounding practices, administration techniques, and the physical constraints of vascular access devices [3]. The American Society of Health-System Pharmacists defines drug incompatibility as the formation of a physical or visual incompatibility and/or the decomposition of one or more components by more than 10% in less than 24 hours under specified conditions [4]. This definition encompasses phenomena ranging from overt precipitation to subtle loss of potency that may escape visual detection entirely [5]. The clinical epidemiology of intravenous drug incompatibility reveals a burden that is both substantial and disturbingly persistent despite decades of awareness [6]. In a prospective algorithm-based analysis of 104 critically ill patients receiving central venous therapy, at least one incompatible drug pair was identified in 64 patients, corresponding to a prevalence of 61.4% [2]. Among 130 incompatible combinations in that analysis, 81 (62.3%) involved piperacillin/tazobactam, with furosemide and pantoprazole each implicated in 18 combinations (13.8%) [2]. Earlier investigators reported that approximately 14% of all medication errors in critical care settings were attributable to incompatibilities, while other estimates have attributed up to 25% of medication errors to this cause [3]. Incompatibilities have been documented in 12% of drug pairs infused in intensive care, and a study of intensive care units in Libya found that 11.5% of patients received incompatible drug pairs while 25.5% received pairs for which compatibility data were unconfirmed [6]. Nearly 19% of drug-related problems in the intensive care unit have been reported to arise from drug incompatibility, and the complications that ensue include central venous catheter occlusion or malfunction, particle embolism due to crystallization or detachment, therapeutic failure, and local or systemic inflammatory reactions [3]. These figures collectively establish intravenous incompatibility as a high-prevalence, high-consequence patient safety concern that demands systematic and sustained pharmacist engagement [1]. The foundational classification of drug incompatibilities distinguishes physical, chemical, and therapeutic categories, each with distinct mechanisms and detection challenges [4]. Physical incompatibilities are the most readily apparent and are evidenced by visible changes such as particulate formation, haze, precipitation, color change, and gas evolution, although subvisible physical reactions including pH shifts, subvisible particle generation, and decreases in drug concentration may occur without any perceptible alteration in the infusion [7]. Chemical incompatibilities result in decomposition of a drug, with a loss of potency exceeding 10% over the defined testing period constituting the threshold, and most chemical incompatibilities can be detected only through suitable analytical methods rather than visual inspection [8]. Therapeutic incompatibilities, in which a drug combination produces undesirable antagonistic or synergistic pharmacologic activity, fall beyond the scope of most compatibility references and require clinical pharmacological judgment that pharmacists are uniquely trained to provide [9]. A change in pH is the primary characteristic involved in drug incompatibilities, but compatibility depends on numerous additional factors including concentration, temperature, storage vehicle, order of mixing, administration technique, and the presence of excipients in a medication [7]. The probability of an incompatibility reaction increases with the duration of contact between drugs, and the concentrations of the respective medications materially influence their compatibility, meaning that the same drug pair may be compatible under one set of conditions and incompatible under another [8]. These mechanistic complexities render reliance on memorized compatibility lists insufficient and instead demand the systematic, evidence-based, and patient-specific approach that pharmacists are positioned to deliver [9]. The clinical consequences of unrecognized or unmanaged intravenous incompatibilities span a continuum from subtle therapeutic failure to catastrophic patient harm, and the pathway from physicochemical reaction to adverse outcome is often indirect and therefore easily overlooked [10]. The formation of

precipitates may partially or completely occlude the catheter, leading to delayed infusion, drug loss, and the need for catheter replacement, while the generation of toxic components and the deposition of particles in key organs including the kidney, liver, and lungs can produce particle-induced mechanical damage to blood vessels and systemic inflammatory response syndromes [3]. Crystals injected into the body can be transported to organs and pose a risk of multiple organ failure, and particulate matter that passes through the infusion line without filtration represents an unavoidable injection of microscopic precipitates during infusion therapy [10]. A published case report documented total occlusion of an intravenous catheter resulting from the incompatibility of remimazolam besylate with Ringer's acetate infusion, illustrating that even relatively recently introduced agents are not exempt from these hazards [7]. The consequences of incompatibility also include therapeutic failure when the active drug is degraded or precipitated before reaching the patient, as well as local or systemic inflammatory reactions that may be misattributed to the underlying disease rather than to the administration process itself [8]. These clinical sequelae translate into measurable economic burden because medication errors generally cause additional interventions, prolonged hospitalization, and higher costs of care, and errors involving intravenously administered drugs have been shown to have more severe consequences and to generate higher costs than errors by other routes [11]. Among intravenous medication administration errors, four error types—wrong diluent mixture, wrong diluent volume, wrong bolus rate, and drug incompatibility—have been reported to account for over 91% of the total [12]. Smart pump data from a large-scale analysis conservatively estimated that catastrophic errors averted would cost US$114,503 per 10,000 infusions delivered, with an average 1,000-bed hospital delivering approximately 750,000 infusions per annum [17]. These economic estimates, while necessarily imprecise, reinforce the case for proactive pharmacist-led prevention as a cost-avoidance strategy rather than merely a quality-improvement aspiration [1].

Mechanisms and Classification of Intravenous Incompatibility

The mechanistic basis of intravenous incompatibility is rooted in the physicochemical behavior of drugs in solution, and pharmacists must understand these mechanisms to interpret compatibility references and to advise on administration [4]. Physical incompatibilities are the most visible and include precipitation, haze, color change, gas evolution, and particulate formation, but subvisible changes such as pH shifts and subvisible particle generation may occur without any perceptible alteration in the infusion [7]. Chemical incompatibilities involve drug decomposition, and the threshold of a loss of potency exceeding 10% over the defined testing period is used to classify a combination as chemically incompatible [8]. Therapeutic incompatibilities involve undesirable pharmacologic antagonism or synergy and are not captured by most physicochemical compatibility databases, which means that pharmacists must apply clinical pharmacological reasoning when evaluating such combinations [9]. A change in pH is the primary characteristic involved in drug incompatibilities, but compatibility also depends on concentration, temperature, storage vehicle, order of mixing, administration technique, and the presence of excipients [7]. The probability of an incompatibility reaction increases with the duration of contact between drugs, and the concentrations of the respective medications materially influence their compatibility [8]. The same drug pair may therefore be compatible under one set of conditions and incompatible under another, which makes context-free compatibility lists insufficient for safe practice [9]. These mechanistic complexities explain why pharmacist review must be patient-specific and administration-specific rather than limited to a binary check of drug names [1]. The presence of excipients in a medication can also contribute to incompatibility, and this dimension is often neglected in simplified compatibility tables [7]. The order of mixing and the administration technique are modifiable factors that pharmacists can influence through compounding guidance and administration recommendations [5]. The duration of contact between drugs is modifiable through sequential administration, line flushing, and the use of multi-lumen catheters, and these strategies fall within the pharmacist's advisory role [3]. The physical consequences of incompatibility are often mediated by particulate load, and the choice of infusion device and the presence of fluid volume support can influence the mass flow rates and particulate burden delivered to the patient [5]. A low common volume line and the use of simulated fluid volume support have been associated with smaller fluctuations in mass flow rate, suggesting that infusion set design is a modifiable factor that can attenuate the physical consequences of incompatibility even when the drug pair itself remains inherently incompatible [5]. The main risk associated with drug incompatibility is partial or complete catheter blockage, which leads to delayed infusion, drug loss, the formation of toxic components, particle deposition in key organs, and particle-induced mechanical damage to blood vessels and systemic inflammatory response syndromes [3]. Strategies that reduce the common volume in which drugs mix can therefore reduce the particulate burden delivered to the patient [5]. Multi-lumen infusion devices and three-port manifolds with extension lines have been evaluated as means of physically separating incompatible drugs, and the major difference between multilumen infusion sets and three-port manifolds resides in the common volume line, that is, the volume from the meeting point between the two drug channels to the end of the catheter [5]. In-line filtration is a further mechanistically plausible strategy for reducing particle exposure, and consensus

recommendations on the clinical use of in-line filtration during intravenous infusions have been developed to guide practice and future research [10]. These mechanistic and engineering considerations are not peripheral to pharmacy practice but constitute the scientific foundation on which pharmacist recommendations about compatibility, sequencing, and infusion-system selection are built [9].

Clinical and Economic Burden

The clinical burden of intravenous incompatibility is best understood through the frequency with which incompatible combinations are prescribed and the severity of the outcomes they can produce [2]. In a prospective algorithm-based analysis of critically ill patients, at least one incompatible drug pair was identified in 61.4% of patients, and piperacillin/tazobactam was the most frequently involved agent [2]. Furosemide and pantoprazole were each implicated in 13.8% of incompatible combinations, which identifies specific drug pairs that should be prioritized in pharmacist-led screening and education [2]. A study of intensive care units in Libya found that 11.5% of patients received incompatible drug pairs while 25.5% received pairs for which compatibility data were unconfirmed [6]. This unconfirmed-data category is particularly important because it reflects the limits of compatibility references and the frequency with which pharmacists must make recommendations under uncertainty [6]. Nearly 19% of drug-related problems in the intensive care unit have been reported to arise from drug incompatibility, and the complications that ensue include central venous catheter occlusion or malfunction, particle embolism due to crystallization or detachment, therapeutic failure, and local or systemic inflammatory reactions [3]. Crystals injected into the body can be transported to organs and pose a risk of multiple organ failure, and particulate matter that passes through the infusion line without filtration represents an unavoidable injection of microscopic precipitates during infusion therapy [10]. A published case report documented total occlusion of an intravenous catheter resulting from the incompatibility of remimazolam besylate with Ringer's acetate infusion, illustrating that even relatively recently introduced agents are not exempt from these hazards [7]. Therapeutic failure occurs when the active drug is degraded or precipitated before reaching the patient, and local or systemic inflammatory reactions may be misattributed to the underlying disease rather than to the administration process itself [8]. These clinical sequelae translate into measurable economic burden because medication errors generally cause additional interventions, prolonged hospitalization, and higher costs of care [11]. Errors involving intravenously administered drugs have been shown to have more severe consequences and to generate higher costs than errors by other routes [11]. Among intravenous medication administration errors, four error types—wrong diluent mixture, wrong diluent volume, wrong bolus rate, and drug incompatibility—have been reported to account for over 91% of the total [12]. Smart pump data from a large-scale analysis conservatively estimated that catastrophic errors averted would cost US$114,503 per 10,000 infusions delivered, with an average 1,000-bed hospital delivering approximately 750,000 infusions per annum [17]. These economic estimates reinforce the case for proactive pharmacist-led prevention as a cost-avoidance strategy rather than merely a quality-improvement aspiration [1]. The burden is therefore both clinical and economic, and it is concentrated in high-acuity settings where polypharmacy and limited vascular access increase the probability of incompatible co-administration [2].

Prescription Review and Compatibility Screening

Pharmacist-led prescription review constitutes the first and most proximal defense against intravenous incompatibility because it intervenes before an incompatible order reaches the patient [1]. The implementation of a pre-issue monitoring program using cloud-based compatibility software in a South Korean general hospital demonstrated that adding intravenous drug prescription review to pharmacists' scope of work was feasible and produced meaningful safety benefits even in the context of chronic pharmacist shortages [1]. In that program, the mean run-time for compatibility review was 18.1 minutes in the intensive care unit and 8.7 minutes in the hematology-oncology ward, and the mean intervention ratio was 25.3% in the intensive care unit versus 5.3% in the hematology-oncology ward [1]. The mean acceptance ratio for pharmacist interventions was 90.4% in the intensive care unit and 100% in the hematology-oncology ward, indicating that prescribers overwhelmingly accepted pharmacist recommendations regarding incompatible combinations [1]. The most frequently triggering incompatible pairs were tazobactam/piperacillin with famotidine in the intensive care unit and vincristine with sodium bicarbonate in the hematology-oncology ward [1]. The authors concluded that despite pharmacist shortages, intravenous compatibility can be monitored before issuing injectable products in all wards, with the caveat that prescribing patterns vary across wards and pharmacists' tasks should be established accordingly [1]. On a per-patient basis, intravenous incompatibility risk occurred once for every four patients in the intensive care unit and once per 19 patients in the hematology-oncology ward, which quantifies the frequency with which pharmacist review intercepts potentially hazardous combinations [1]. The effectiveness of pharmacist review is inseparable from the quality and accessibility of compatibility information resources [6]. Compatibility data are retrieved from multiple sources

including Summaries of Product Characteristics, Stabilis, Trissel's IV Compatibility, and the KIK database, and discrepancies among these sources can create uncertainty when pharmacists adjudicate the acceptability of a given combination [6]. Trissel's 2 Clinical Pharmaceutics Database provides in-depth content on the properties of more than 850 drugs and solutions and yields over 76,500 compatibility results encompassing Y-site, admixture, solution, and syringe administration [8]. Such comprehensive resources are indispensable for evidence-based decision-making, but the absence of confirmed compatibility data for a substantial proportion of drug pairs means that pharmacists frequently must make recommendations under uncertainty [8]. The study of pharmacists' monitoring for intravenous drug compatibility explicitly acknowledged this gap and noted that efforts to generate more evidence should continue to improve the completeness of information available to support clinical decisions [1]. Clinical pharmacist participation in interdisciplinary rounds amplifies the impact of prescription review by embedding compatibility assessment within therapeutic decision-making [19]. Nurses and pharmacists can work together to prevent medication errors by checking medication compatibility, continuously monitoring patient reactions, and revising compatibility recommendations [20]. Pharmacists examine prescriptions to avoid contraindicated drug combinations while nurses, as frontline caretakers, ensure that drugs are administered correctly [20]. Approximately 50% of pharmaceutical mistakes are caused by physicochemical interactions, particularly in intravenous dose forms, and this coordinated approach is critical for reducing prescription mistakes while improving the stability and efficacy of pharmacological formulations [20]. The Integrated Management Model of Doctor-Nurse-Pharmacist Collaboration has been shown to significantly reduce the incidence of drug incompatibility in intravenous treatment for critically ill patients [22]. One analysis reported a decrease in the incidence of drug compatibility contraindications from 3.5% to 1.5% following implementation of the integrated model [22]. Such findings confirm that the pharmacist's contribution is not confined to order verification but extends to active participation in therapeutic plan optimization [22].

Compounding, Standardization, and Infusion-System Design

The compounding and preparation phase represents a critical control point at which pharmacists can prevent incompatibility through formulation and process design [11]. The 2022 ISMP Guidelines for Sterile Compounding and the Safe Use of Sterile Compounding Technology focus on essential technology attributes, safe pharmacy processes, and safety gaps in three areas, and they establish expectations for intravenous workflow management systems that document all steps and components of the compounding process [11]. USP <797> standards, aligned with ASPEN and ASHP guidance, govern safe intravenous admixture and compounding practices, and staff in intravenous compounding spaces undergo compounding review to understand the complexities of sterility as well as stability and compatibility [18]. The application of these standards is particularly consequential for parenteral nutrition, where the simultaneous presence of numerous components creates a high risk of physicochemical incompatibility [18]. The education and training of pharmacists in parenteral nutrition compounding remain an area of documented challenge and ongoing refinement [18]. The 2022 ISMP guidelines and the associated sterile compounding technology standards therefore constitute a foundational infrastructure within which pharmacists exercise their responsibility for ensuring that the preparation process itself does not introduce or exacerbate incompatibility hazards [11]. Standardization of intravenous drug concentrations and administration protocols offers a complementary strategy for reducing incompatibility risk by limiting unnecessary variability in the conditions under which drugs are combined [12]. National and international initiatives have produced standardized concentration lists for continuous infusions in intensive care, with one German multidisciplinary effort publishing a list of 41 active substances and 49 standard concentrations including suitable carrier solutions and physicochemical stability data [12]. This list represents an essential building block for improving drug therapy safety [12]. The 2022–2023 ISMP Targeted Medication Safety Best Practices for Hospitals similarly emphasize standardization of how drug concentrations, doses, and rates are expressed, recognizing that variability in these parameters contributes to error and incompatibility risk [13]. Ready-to-administer products represent a further standardization strategy, and the transition from vial-to-syringe preparation to manufacturer-prepared prefilled products has been discussed in terms of both safety and affordability [14]. Reducing the number of manipulation steps in the preparation process diminishes the opportunity for incompatible combinations and concentration errors to arise [14]. The pharmacist's role in formulary decision-making and product selection is therefore directly relevant to incompatibility prevention because the choice of presentation format and concentration standard determines the range of combinations that are practically feasible at the point of administration [14]. Dilution and infusion set design constitute additional pharmacist-influenced variables that modulate the physical interaction between incompatible drugs within the infusion line [5]. An in vitro study examining simultaneous infusion of vancomycin and piperacillin/tazobactam found that mass flow rates were primarily influenced by the choice of infusion device and the presence of simulated fluid volume support [5]. The dynamic particulate load increased during flow rate changes,

especially in infusion sets with a large common volume line and no concomitant fluid volume support [5]. A low common volume line and the use of simulated fluid volume support were associated with smaller fluctuations in mass flow rate, suggesting that infusion set design and fluid support are modifiable factors that can attenuate the physical consequences of incompatibility even when the drug pair itself remains inherently incompatible [5]. Multi-lumen infusion devices and three-port manifolds with extension lines have been evaluated as means of physically separating incompatible drugs, and the major difference between multilumen infusion sets and three-port manifolds resides in the common volume line [5]. These engineering considerations fall squarely within the pharmacist's purview when advising on infusion system selection and administration sequencing [5].

Technology-Enabled Safeguards: CPOE, Smart Pumps, and Clinical Decision Support

Computerized prescriber order entry and clinical decision support systems have transformed the pharmacist's capacity to detect and prevent incompatibility at the point of prescribing [15]. In the manual era, pharmacists were often gatekeepers located in the central pharmacy, but with computerized prescriber order entry and integrated electronic health records, pharmacists can virtually round on patients, review orders in real time, and identify errors before the nurse administers the drug [15]. The clinical pharmacy model enabled by computerized prescriber order entry allows infusion pumps to be programmed directly from the order, eliminating manual programming errors entirely [15]. This integration creates opportunities for compatibility alerts to be embedded in the order-entry workflow itself [15]. The effectiveness of computerized prescriber order entry-based compatibility screening depends on the sophistication of the underlying rules and the extent to which alerts are tailored to the clinical context [15]. Excessive or poorly calibrated alerts contribute to alert fatigue and the overriding of clinically significant warnings [15]. The pharmacist's role in computerized prescriber order entry governance—including the development, validation, and maintenance of compatibility alert rules—is therefore a critical and expanding responsibility that bridges informatics and clinical practice [15]. Smart infusion pumps with drug error reduction systems constitute a further technological layer through which pharmacists prevent incompatibility-associated harm, although the primary focus of these systems is dose and rate error rather than physicochemical compatibility per se [16]. A pharmacy-driven performance improvement initiative to increase compliance with intravenous smart pump drug error reduction systems at a large urban academic medical center demonstrated that pharmacist leadership can meaningfully improve drug library compliance [16]. The incorporation of a drug library in an infusion system is the first step in migrating a conventional infusion pump into a smart pump [16]. The drug library compliance rate in one reported initiative was 92%, far superior to data published by other authors reporting percentages around 30–40%, suggesting that pharmacy-driven oversight can overcome the complacency that often undermines technology-based safeguards [16]. Smart pumps have been shown to reduce errors, but they prevent only some programming errors, and compliance rates are negatively influenced by improper smart pumps and the overriding of soft alerts, which can cause alert fatigue and drug library update delays [16]. The pharmacist's involvement in smart pump library review and revision is particularly important in specialty areas such as hematology-oncology, where the impact of a review of a smart infusion pump library tailored to meet specialty needs has been documented as a means of addressing near-miss events and improving the relevance of the safety net [16]. The integration of compatibility data into smart pump systems and electronic health records remains incomplete, and the literature identifies several unresolved challenges that limit the effectiveness of technology-enabled safeguards [15]. The implementation of smart pump technology requires the formation of a multidisciplinary team comprising nurses, doctors, technicians, and pharmacists, and the implementation process is most successful when led by pharmacy [16]. Wireless pump technology has enabled access to smart pump therapy library log data from lower-acuity areas of care such as oncology infusion centers, labor and delivery units, and medical-surgical wards [17]. The incidence of moderate and catastrophic intravenous therapy administration errors outside critical care may be higher than previously recognized, and limited clinician experience with certain medications contributes to error risk [17]. The cost savings associated with smart intravenous technology—conservatively estimated at US$114,503 per 10,000 infusions for catastrophic errors averted—indicate the potential value of deploying such technology in every part of the hospital [17]. Pharmacists are the professionals best positioned to justify and guide this investment through their understanding of medication safety economics and their direct involvement in technology selection and configuration [17]. Technology cannot substitute for clinical judgment, and the pharmacist's role in interpreting compatibility alerts, distinguishing clinically significant from trivial warnings, and providing context-specific recommendations remains indispensable [1].

Education, Interdisciplinary Collaboration, and Cultural Change

Knowledge deficits among prescribers and nurses constitute a modifiable contributor to intravenous incompatibility that pharmacist-led education can address [2]. In a staff survey conducted alongside an algorithm-based analysis of incompatibilities,

37.8% of staff members participated, and the combination of piperacillin/tazobactam and pantoprazole was incorrectly judged to be compatible by 85.7% of respondents [2]. This finding is striking because piperacillin/tazobactam was the drug most frequently involved in incompatible combinations in the patient cohort [2]. Only rarely did the majority of respondents feel unsafe in administering drugs, with a median score of 1 on a scale from 0 (never) to 5 (always), and knowledge deficits correlated well with the incompatibilities identified [2]. The staff therefore did not perceive the risk that their knowledge gaps created [2]. Technical interventions such as prescription review and smart pump safeguards are necessary but insufficient if the frontline workforce lacks the knowledge and risk perception to recognize incompatibility hazards and to adhere to pharmacist recommendations [2]. Pharmacist-delivered education that targets specific knowledge gaps—such as the incompatibility of commonly co-administered agents like piperacillin/tazobactam with pantoprazole or furosemide—can raise awareness and improve the safety culture within which intravenous medications are prescribed and administered [2]. Interdisciplinary collaboration is the organizational mechanism through which pharmacist expertise is translated into practice change [20]. The roles of nurses and pharmacists in reducing physicochemical drug interaction and improving patient safety are complementary because pharmacists examine prescriptions to avoid contraindicated combinations while nurses ensure correct administration and monitor for adverse reactions [20]. Both professionals must work together to discover and avoid physicochemical incompatibilities [20]. The Integrated Management Model of Doctor-Nurse-Pharmacist Collaboration has been associated with significant reductions in catheter-related bloodstream infections and drug incompatibility [22]. The involvement of clinical pharmacists has been shown to enhance medication safety management and effectively prevent adverse drug events [19]. Interdisciplinary collaboration between nurses and pharmacists leads to a reduction in medication errors [20]. The implementation of pharmacist monitoring for intravenous drug compatibility in a real-world hospital setting required active cooperation with prescribers and nurses to ensure that interventions were accepted and acted upon [1]. The pharmacist's role as a collaborator rather than a gatekeeper is therefore essential because recommendations that are perceived as supportive and evidence-based are more likely to be accepted [1]. Recommendations imposed without explanation or contextual understanding may be resisted or ignored [1]. Cultural change at the organizational level is required to sustain pharmacist-led incompatibility prevention [21]. Although infusion therapy is standardized in intensive care units to varying degrees, there are fewer standards regarding administering drugs via multi-lumen catheters [21]. In multidisciplinary teams, the absence of clear protocols for catheter lumen assignment and drug sequencing creates opportunities for incompatible combinations to be infused [21]. The probability of an incompatibility reaction increases with the time of contact between drugs, and the lack of standardized procedures for flushing lines between administrations or for sequencing incompatible drugs means that preventable exposures continue to occur [8]. The development of a 4-step avoidance recommendation in one critical care study—encompassing sequential administration, use of another lumen, taking a break, and use of catheters with more lumens—demonstrates that practical, tiered strategies can be formulated [2]. When such recommendations are provided by pharmacists, they are fully accepted by the clinical team [2]. In that study, all 68 avoidance recommendations given to 64 patients with at least one incompatibility were fully accepted, with sequential administration recommended in 64.7% of cases, use of another lumen in 13.2%, taking a break in 10.3%, and use of catheters with more lumens in 11.8% [2]. The pharmacist's recommendation is therefore not merely advisory but is acted upon when it is specific, feasible, and grounded in compatibility evidence [2]. The translation of pharmacist knowledge into accepted practice change is thus a function of both the quality of the recommendation and the relational and organizational context in which it is delivered [22]. Systematic reviews of drug incompatibility in intensive care have repeatedly identified the need for standardized protocols, improved compatibility databases, and interdisciplinary education as core implementation priorities [21]. Pharmacist-led education and audit can therefore be framed as organizational interventions that address both knowledge deficits and system failures rather than as isolated training events [22].

Table 1. Studies of Pharmacist-Led and Pharmacist-Supported Interventions to Prevent Intravenous Medication Incompatibility Complications

Study (Year)	Setting and Design	Key Pharmacist Role or Intervention	Principal Findings Relevant to Incompatibility Prevention
Cheon et al. (2023) [1]	General hospital, South Korea; prospective analysis of pre-issue compatibility monitoring	Pharmacist review of intravenous prescriptions using cloud-based compatibility software before product issue	Intervention ratios of 25.3% in the intensive care unit and 5.3% in hematology-oncology; acceptance ratios of 90.4% and 100%, respectively;

			feasibility demonstrated despite pharmacist shortage [1]
Wagner et al. (2023) [2]	Critical care; algorithm-based analysis with staff survey	Pharmacist-developed algorithm identifying incompatibilities and generating 4-step avoidance recommendations	At least one incompatibility in 61.4% of patients; 68 recommendations fully accepted; sequential administration most common recommendation at 64.7% [2]
Pehlivanlı et al. (2022) [3]	Intensive care unit; review of incompatibility and Y-site management	Pharmacist awareness of Y-site incompatibility and management strategies	Nearly 19% of drug-related problems in intensive care caused by incompatibility; complications include catheter occlusion, particle embolism, therapeutic failure, and inflammatory reactions [3]
Aljaber and Waterson (2022) [17]	Smart pump log analysis across adult units outside critical care	Pharmacy-led smart pump data review and cost analysis of averted errors	Catastrophic errors averted conservatively cost US$114,503 per 10,000 infusions; smart intravenous technology valuable across all hospital areas [17]
Integrated Management Model study (2024) [22]	Critically ill patients receiving intravenous treatment	Doctor-nurse-pharmacist collaborative model	Incidence of drug compatibility contraindications decreased from 3.5% to 1.5% [22]
Maison et al. (2019) [21]	Intensive care practice evaluation	Pharmacist-supported evaluation of intravenous incompatibility practices	Identified need for standardized protocols, improved compatibility databases, and interdisciplinary education [21]

CONCLUSION

Intravenous medication incompatibility is a significant contemporary patient safety issue, particularly in critical care settings where factors like polypharmacy and high-acuity prescribing are prevalent. Pharmacists play a crucial role in mitigating these risks through various interventions, such as prescription reviews and interdisciplinary education, demonstrating effective results in practice. However, challenges remain, including knowledge gaps among healthcare professionals and limitations in existing technology. Future efforts should focus on enhancing compatibility data, integrating decision support systems, increasing pharmacist involvement in patient care rounds, and assessing patient outcomes related to incompatibility prevention. As intravenous therapy becomes more complex, the pharmacist's role is expected to grow, highlighting the need for investment in staffing and training to reinforce safety in intravenous drug administration.

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