Indigenous Drug Delivery Systems for Battlefield Trauma: Supply-Chain Resilience and Self-Reliance in Military Medicine

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ABSTRACT
Uncontrolled haemorrhage remains the leading cause of potentially survivable death on the battlefield, and the majority of such deaths occur before a casualty reaches surgical care. This has shifted the centre of gravity in military trauma from the operating theatre to the point of injury, where the decisive factor is no longer the availability of a drug molecule but the delivery platform that places it into a bleeding, hypothermic, and often unmonitored patient within the golden hour. This review surveys the principal classes of battlefield-oriented drug delivery systems topical haemostatic dressings, freeze-dried and reconstitutable plasma, antifibrinolytic regimens, self-administered auto-injectors, and thermostable field formulations and evaluates their evidence base and logistical characteristics. It then examines the Indian landscape, where indigenous capability exists in pockets (a domestically manufactured chitosan haemostat and Defence Research and Development Organisation combat-casualty formulations) but coexists with a heavy dependence on imported active pharmaceutical ingredients, excipients, packaging, and cold-chain components. The central argument is that the binding constraint on India's battlefield pharmaceutical readiness is not the ability to achieve a finished delivery device but the resilience of the upstream supply chain that sustains it under wartime conditions. Reframing the problem in these terms aligns military medical procurement with the broader Atmanirbhar Bharat agenda and identifies priorities indigenous plasma lyophilisation, domestic API and excipient capacity, thermostable formulation science, and DRDO industry co-development that would convert episodic self-reliance into a durable strategic capability.

Keywords: Drug delivery systems; Battlefield trauma; Haemostatic dressings; Freeze-dried plasma; Tranexamic acid; Supply-chain resilience; Atmanirbhar Bharat; Military medicine.
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1. Introduction

Haemorrhage is the principal cause of preventable death in armed conflict. In the United States campaigns in Afghanistan and Iraq, approximately nine in ten combat fatalities died before reaching a surgical facility, and around nine in ten of the deaths judged potentially survivable were attributable to bleeding.[1] The anatomical distribution of these deaths is instructive: the largest fraction arises from truncal (non-compressible) haemorrhage, followed by junctional and extremity sites (Figure 1).[1] Because a tourniquet can address only compressible extremity bleeding, the deaths that dominate the statistics are precisely those that conventional first aid cannot reach, which is why pharmacological haemorrhage control has become the defining problem of forward trauma care.

The operational consequence is a compression of the therapeutic timeline. Survival and the avoidance of long-term disability are greatest when effective intervention is delivered within the first hour after wounding the so-called golden hour yet the battlefield is the most hostile imaginable setting in which to administer a drug.[2] Care is frequently rendered by a single medic, or by the casualty themselves, under fire, in darkness, at altitude, or in extreme cold, without laboratory support, refrigeration, or a controlled airway. In this environment the scientific challenge is not principally the discovery of new active molecules, most of which already exist, but the engineering of delivery systems that make those molecules usable: dressings that clot blood on contact, plasma that can be stored on a shelf and reconstituted in minutes, antifibrinolytics that a

medic can give without monitoring, and antidotes that a soldier can self-inject through clothing.

This review approaches battlefield drug delivery as a problem of military logistics and strategic self-reliance rather than of formulation chemistry alone. It first outlines the constraints that define the point-of-injury environment, then surveys the major delivery classes and their evidence base, and finally examines the Indian position, where indigenous capability is real but uneven and where the decisive vulnerability lies upstream in the supply chain. The argument advanced is that finished-device capability and supply-chain resilience are distinct problems, and that India's battlefield pharmaceutical readiness will be determined by the latter.

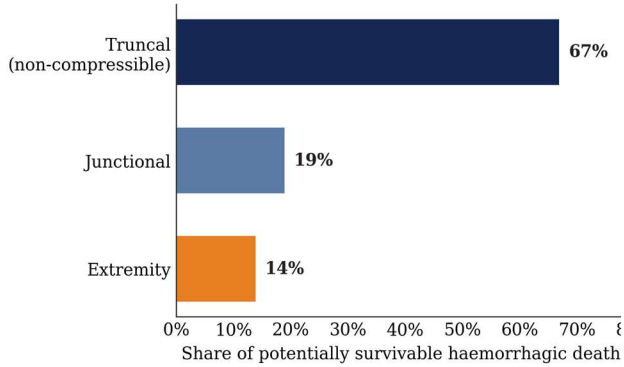

Figure 1. Approximate anatomical distribution of potentially survivable haemorrhagic deaths in combat, showing the predominance of non-compressible truncal bleeding. [[1]]

2. The Point-of-Injury Pharmacological Challenge

Five constraints distinguish battlefield drug delivery from hospital pharmacotherapy. First, non-compressibility: the highest-yield targets are torso and junctional wounds where external pressure is ineffective, demanding agents that act intraluminally or at the wound surface.[1] Second, the operator: interventions must be simple enough for a combat medic or an injured soldier to perform reliably under stress, which favours pre-filled, single-action devices over multi-step preparation. Third, the thermal environment: aqueous formulations degrade at high temperature and may freeze at altitude, so a product's real-world shelf life is governed as much by its thermal tolerance as by its chemistry.[2] Fourth, time: several of the most effective interventions are strongly time-dependent, losing much of their benefit if delayed beyond the first hours. Fifth, logistics: any product that requires refrigeration imposes a cold chain that is difficult to sustain across dispersed, mobile, and contested forces. A delivery system is therefore judged not only by its pharmacological efficacy but by whether it can survive storage, transport, and administration in the field—criteria that repeatedly favour solid, thermostable, and self-contained formats over conventional liquids.

3. Advances in Battlefield Drug Delivery Systems

3.1 Topical haemostatic delivery platforms

Topical haemostatic dressings are the most mature class of battlefield delivery technology. Two mechanisms dominate: mineral concentrators such as kaolin, which accelerate the intrinsic coagulation cascade, and biopolymers such as chitosan, a deacetylated derivative of chitin that is mucoadhesive, promotes erythrocyte and platelet aggregation independently of the patient's own clotting factors, and carries useful broad-spectrum antibacterial activity.[3] The first chitosan dressing, HemCon, was fielded for United States forces in Afghanistan and Iraq from 2003, and subsequent chitosan gauzes (Celox and ChitoGauze) were incorporated into the Tactical Combat Casualty Care guidelines alongside kaolin-impregnated Combat Gauze after animal and clinical evidence showed them to be at least equally efficacious.[4] In a swine femoral-artery model, a chitosan gauze reduced blood loss several-fold relative to standard gauze in the surviving animals, illustrating the magnitude of benefit achievable from a delivery format as simple as an impregnated dressing.[5] Importantly for this review, one of the clinically validated chitosan haemostats is manufactured in India: a domestic randomised pre-hospital study of 104 patients with bleeding wounds compared an Indian chitosan dressing with conventional cotton gauze during ambulance transport, demonstrating faster haemostasis and reduced blood loss.[6] Beyond dressings, expandable compressed-sponge injectors have been developed for narrow, deep junctional wounds that gauze cannot pack, extending the same contact-haemostasis principle into a new delivery geometry.[7] A comparison of representative platforms is given in Table 1.

Table 1. Representative battlefield topical haemostatic delivery platforms.

Product (example)	Active principle / mechanism	Delivery format	Origin
Combat Gauze	Kaolin; contact activation of intrinsic pathway	Impregnated rolled gauze	USA
Celox / ChitoGauze	Chitosan; factor-independent cell	Impregnated gauze	UK / USA

Product (example)	Active principle / mechanism	Delivery format	Origin
	aggregation		
HemCon	Chitosan; mucoadhesive wound sealing	Rigid patch / bandage	USA
Axiostat (indigenous)	Chitosan; factor-independent haemostasis	Dressing / pad	India
Compressed-sponge injector	Mechanical tamponade of deep tracts	Applicator-delivered sponges	USA

3.2 Freeze-dried plasma and reconstitutable biologics

Early transfusion of plasma improves survival in haemorrhagic shock, but fresh frozen plasma is impractical forward of a hospital because it must be kept frozen, thawed, and blood-group matched. Lyophilisation solves the delivery problem: freeze-dried plasma (FDP) is a powder that is stable at ambient temperature, requires no blood typing, and can be reconstituted in a few minutes at the point of care. FDP is not new it was developed by the United States Army during the Second World War but it was European military services that sustained the capability, the French Armed Forces producing lyophilised plasma continuously and fielding a pathogen-reduced product that is storable at room temperature for around two years and reconstituted in under six minutes.[8,9] Controlled animal work shows that the lyophilisation–reconstitution cycle reduces clotting-factor activity by only about fourteen per cent while preserving haemostatic efficacy comparable to fresh frozen plasma.[10] Randomised prehospital trials of dried and liquid plasma in trauma have since been conducted, and although results on mortality are mixed and context-dependent, the logistical case for a shelf-stable plasma remains compelling for austere and military settings.[11] Several national products now exist French lyophilised plasma, the German single-donor LyoPlas, and a South African pooled product each differing in donor pooling and pathogen-reduction strategy (Table 2).[12] India has no comparably established indigenous FDP capability, a gap discussed in Section 4.

Table 2. Selected national freeze-dried / lyophilised plasma programmes.

Product	Country	Storage & reconstitution	Notable feature
French lyophilised plasma (FLYP)	France	Ambient, ~2 yr; reconstituted <6 min	Pooled multi-donor; pathogen-reduced; universal
LyoPlas	Germany	Ambient; rapid reconstitution	Single-donor; quarantine-stored
Bioplasma FDP	South Africa	Ambient; rapid reconstitution	Large-pool, solvent/detergent, ABO-universal
FDP (fielded)	USA	Ambient; rapid reconstitution	Historically French-sourced for far-forward use

3.3 Antifibrinolytic delivery: tranexamic acid

Tranexamic acid (TXA), a lysine analogue that inhibits fibrinolysis, is attractive for forward use because it is inexpensive, does not require refrigeration in its usual presentation, and can be given by a medic without laboratory monitoring. The CRASH-2 trial randomised more than twenty thousand trauma patients across 274 hospitals in forty countries and found that early TXA reduced all-cause mortality (14.5 per cent versus 16.0 per cent) and death due to bleeding, with a number needed to treat of around 67 for overall mortality.[13] The military MATTERs analysis reported a larger absolute mortality benefit in a combat-injured cohort, supporting the incorporation of TXA into military trauma protocols.[14] The benefit is, however, sharply time-dependent greatest within the first hour and largely lost after three hours and is not free of thromboembolic risk, so the delivery objective is early, protocolised administration rather than universal use.[15] TXA illustrates a general point: the value of a molecule at the point of injury is realised only through a delivery and decision system that gets it into the patient quickly.

3.4 Auto-injectors and self-administered countermeasures

Where a soldier must treat themselves within minutes, the spring-loaded auto-injector is the archetypal delivery device. The canonical case is nerve-agent poisoning, for which the antidotes atropine and pralidoxime chloride are delivered

intramuscularly through clothing by self- or buddy-aid, historically as the two-chamber MARK I kit and later as the single-needle ATNAA.[16] These devices also expose a characteristic vulnerability of liquid-filled delivery systems: the aqueous antidote must be stored within a narrow temperature band and protected from freezing, constraining stockpiling in hot or high-altitude theatres.[16] India has pursued indigenous auto-injector development, including work to combine atropine sulphate and pralidoxime chloride in a single cartridge and to characterise the stability of that combination an example of domestic delivery-device engineering with direct defence relevance.[17] The same platform is applicable to self-administered analgesia and other emergency drugs, making auto-injector manufacturing a strategically significant capability in its own right.

3.5 Thermostable and cold-chain-independent formulations

The recurring theme across the preceding classes is that thermal tolerance, not intrinsic potency, often decides field utility. This has driven a distinct line of formulation work aimed at removing the cold chain. Freeze-drying is one route, as with plasma; reformulation of the vehicle is another. Indian defence laboratories have, for instance, developed a glycerated saline resuscitation fluid that resists freezing to around minus eighteen degrees Celsius for use in high-altitude trauma, alongside wound sealants and super-absorptive dressings intended to extend the golden hour until evacuation.[18] Such thermostable formulations are unglamorous but strategically decisive, because they determine whether a product remains usable after weeks of dispersed storage in the conditions that Indian forces actually operate in, from desert heat to Himalayan cold.

4. The Indian Landscape: Indigenous Capability and Import Dependence

India's battlefield pharmaceutical position is a study in contrasts. On the capability side, indigenous assets are genuine. A domestically manufactured chitosan haemostat has clinical validation and is in civilian and para-military use;[6] the Defence Research and Development Organisation, through its life-sciences laboratories, has developed a suite of combat-casualty formulations including bleeding-wound sealants, super-absorptive dressings, and the cold-resistant glycerated saline noted above;[18] and Indian groups have engineered indigenous nerve-agent auto-injectors.[17] The Armed Forces Medical Services have long clinical experience of managing penetrating and blast trauma in counter-insurgency and high-altitude settings, providing the operational knowledge base into which these products fit.[19,20]

The vulnerability lies upstream. India remains heavily dependent on imported active pharmaceutical ingredients (APIs) by common estimates around seventy per cent of bulk-drug requirements overall, rising to as much as ninety per cent for certain critical categories such as selected antibiotics and cardiovascular agents with a large share sourced from a single external supplier.[21] The pattern extends to medical devices, of which an estimated seventy to eighty per cent are imported, including high-value and critical items (Figure 2).[22] Excipients, specialised packaging, and cold-chain equipment show similar import intensity. The strategic implication is direct: a finished haemostatic dressing or auto-injector assembled in India may still depend, ingredient by ingredient, on supply lines that a conflict or an export restriction could sever. Recognising this, the Government has advanced a series of self-reliance measures under the Atmanirbhar Bharat framework, including the Production-Linked Incentive scheme for bulk drugs and the bulk-drug parks initiative to rebuild domestic API capacity,[23] and larger research-and-innovation schemes for the pharmaceutical and med-tech sector.[24] These are necessary, but they are oriented at the civilian pharmaceutical economy; their translation to defence-specific countermeasures is not automatic. Table 3 summarises the indigenous status of the main capability areas discussed here.

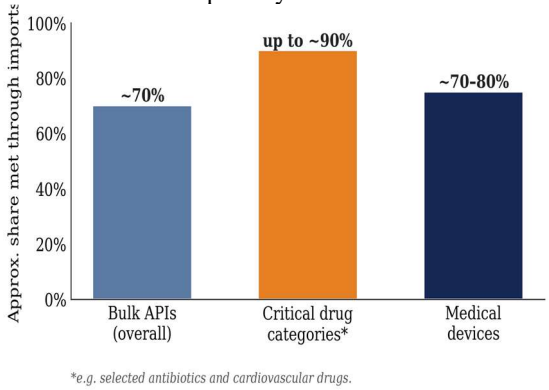

Figure 2. Approximate share of India's pharmaceutical and medical-device inputs met through imports, illustrating the upstream supply-chain exposure behind nominally indigenous finished products. [[21]] [[22]]

Table 3. Indicative indigenous status of key battlefield drug-delivery capabilities in India.

Capability area	Indigenous status	Principal actor(s)	Binding gap
Topical chitosan haemostats	Established, clinically validated	Domestic manufacturer	Chitosan / raw-material sourcing

Capability area	Indigenous status	Principal actor(s)	Binding gap
Combat-casualty field formulations	Developed	DRDO life-sciences labs	Scale-up & procurement pathway
Nerve-agent auto-injectors	Developed / prototyped	DRDO / defence R&D	Device components & API supply
Freeze-dried plasma	No established indigenous product	—	Lyophilisation & regulatory capacity
APIs, excipients, packaging	Largely import-dependent	Private pharma (civilian)	Upstream self-sufficiency

5. Reframing the Problem: Supply-Chain Resilience as the Core Vulnerability

The evidence assembled above supports a specific reframing. The dominant narrative of self-reliance tends to equate capability with the ability to display a finished product a dressing, a device, a fluid bearing an indigenous label. Yet the analysis of Sections 3 and 4 shows that finished-device capability and wartime availability are different things. A delivery platform is the visible tip of a chain that runs backwards through the active ingredient, the excipient, the specialised packaging, the sterilisation and lyophilisation equipment, and the cold-chain and quality infrastructure that sustain it. Battlefield readiness is set by the weakest link in that chain, not by the existence of the end product. India can, and does, manufacture chitosan dressings and auto-injectors; whether it can continue to do so at scale during a prolonged conflict, when imported APIs, reagents, or device components are interdicted, is a separate and more demanding question.

This is the same structural insight that recurs across defence-industrial analysis: the achievement of an assembled system an airframe, a device can mask a dependency that resides in its supply chain rather than in its design. Applied to military medicine, it implies that the appropriate metric of self-reliance is not the count of indigenous products but the depth of indigenous control over the inputs those products require under stress. Framing battlefield drug delivery as a supply-chain resilience problem rather than a device-availability problem changes the policy target: from procuring finished countermeasures to securing the upstream capacity API synthesis, excipient and packaging manufacture, plasma lyophilisation, thermostable formulation science, and the associated regulatory throughput without which finished countermeasures cannot be reliably produced when they are most needed.

6. Challenges

Several obstacles stand between the present position and a resilient indigenous capability. Regulatory throughput is one: biologics such as lyophilised plasma and combination auto-injectors face demanding approval and quality pathways, and domestic capacity to evaluate and license them at speed is limited. Manufacturing scale is another: pilot or laboratory-scale success at DRDO or in academia does not translate automatically into sustained mass production, which requires a procurement pathway that pulls products through to the field. The cold chain and thermal robustness remain a persistent engineering challenge for liquid formulations and biologics alike. Dual-use sensitivity complicates the sharing of certain countermeasure technologies and can restrict access to inputs. The evidence base is itself contested for some interventions the mortality benefit of prehospital plasma and the boundaries of TXA use are still debated[1115] so indigenisation must be paired with domestic clinical and preclinical research rather than mere copying. Finally, the civilian orientation of current self-reliance schemes means defence-specific requirements, such as extreme-temperature stability and buddy-aid usability, may be under-served unless explicitly incorporated.

7. Future Perspectives

Four priorities follow from the supply-chain framing. First, indigenous plasma lyophilisation: establishing a domestic freeze-dried plasma capability, drawing on the well-documented French and German models, would close the most conspicuous gap in India's far-forward resuscitation chain.[8] Second, upstream self-sufficiency in inputs: extending the logic of the bulk-drug parks and Production-Linked Incentive schemes explicitly to the APIs, excipients, and device components required for military countermeasures would convert nominal finished-product self-reliance into real resilience.[23] Third, thermostable formulation science: sustained investment in freeze-dried, depot, and cold-tolerant formats building on demonstrated Indian work such as glycerated saline directly addresses the thermal constraint that most often defeats field delivery.[18] Fourth, an institutional pathway: structured DRDO–industry co-development, coupled with strategic stockpiling and defence-specific standards, would bridge the gap between laboratory prototype and fielded product. Emerging delivery science nanocarrier and hydrogel systems for controlled release, intranasal and

transdermal routes that avoid injection, and freeze-dried whole-blood analogues offers a longer-term horizon, but its strategic value for India will again depend less on the novelty of the platform than on whether its supply chain can be domesticated.

8. Conclusion

Battlefield trauma care has moved decisively toward the point of injury, and with it the importance of drug delivery systems that place haemostatic, resuscitative, and antidotal therapy into casualties within the golden hour. The technologies exist and are increasingly mature, from chitosan and kaolin dressings to freeze-dried plasma, protocolised tranexamic acid, and self-administered auto-injectors. India possesses genuine but uneven indigenous capability across these classes. The argument of this review is that the decisive constraint on India's battlefield pharmaceutical readiness is not the achievement of finished delivery devices but the resilience of the supply chain that sustains them. Recognising that finished-product capability and supply-chain security are distinct problems reorients the self-reliance agenda toward the upstream inputs active ingredients, excipients, packaging, lyophilisation, and thermostable formulation whose domestication would turn episodic indigenisation into a durable strategic capability in military medicine.

Declarations

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