DERLEME

*Osmangazi Tıp Dergisi Öğrenci Özel Sayısı* *DOI: 10.20515/otd.1990954*

# Topical Haemostatic Agents In Modern Surgery: A Mechanism-Oriented Classification

## Modern Cerrahide Topikal Hemostatik Ajanlar: Mekanizma Odaklı Bir Sınıflandırma

Salih Ceylan[1], Erhan Kürkçüoğlu[2], Turan Kandemir[2]

[1]Eskişehir Osmangazi University, Faculty of Medicine, Medical Student, Eskişehir, Türkiye
[2]Eskişehir Osmangazi University, Faculty of Medicine, Neurosurgery, Eskişehir, Türkiye

**Özet:** Hemostaz, doku hasarı sonrasında vasküler bütünlüğü koruyan, vasküler yanıtlar, trombosit aktivasyonu ve pıhtılaşma kaskadı etkileşimlerini içeren karmaşık fizyolojik bir süreçtir. Cerrahi tekniklerdeki ve perioperatif bakımdaki önemli gelişmelere rağmen, intraoperatif ve postoperatif kanamalar modern cerrahide temel zorluklar olmaya devam etmektedir. Sonuç olarak, topikal hemostatik ajanlar basit pasif materyallerden biyolojik olarak aktif, akışkan, mastik bazlı ve rejeneratif platformlara evrilmiştir. Bu derleme, pıhtılaşmanın fizyolojik temeliyle entegre yapılandırılmış bir sınıflandırma çerçevesi aracılığıyla topikal hemostatik ajanlara ve bunların klinik uygulamalarına mekanizma odaklı bir genel bakış sunmaktadır. Günümüzde mevcut olan topikal hemostatik ajanların naratif bir derlemesi yapılmış olup, ajanlar materyal bileşimi, etki mekanizması ve fonksiyonel özelliklerine göre beş ana kategoriye ayrılmıştır: mekanik iskele hemostatik ajanlar, biyolojik olarak aktif hemostatik ajanlar, akışkan hemostatik ajanlar, örtücü/yapıştırıcı hemostatik ajanlar ve gelişmekte olan rejeneratif hemostatik teknolojiler. Mekanik iskele ajanlar rutin kanama kontrolü için temel araçlar olmaya devam ederken, biyolojik olarak aktif ve akışkan hemostatlar karmaşık kanama ortamlarında artmış etkinlik sunar. Örtücü ve yapıştırıcı hemostatlar işlevselliği hemostazın ötesine taşıyarak doku takviyesi ve sızıntı önlemeye kadar genişletir. Gelişmekte olan rejeneratif teknolojiler, kanama kontrolünü doku onarımı ile entegre edebilecek gelişen bir sınırı temsil etmektedir.
**Anahtar Kelimeler:** Topikal hemostatik ajanlar, hemostaz, cerrahi kanama, pıhtılaşma kaskadı

**Abstract:** Haemostasis is a complex physiological process involving vascular responses, platelet activation and coagulation cascade interactions that collectively maintain vascular integrity following tissue injury. Despite substantial advances in surgical techniques and perioperative care, intraoperative and postoperative bleeding remain major challenges in modern surgery. Consequently, topical haemostatic agents have evolved from simple passive materials to advanced biologically active, flowable, sealant-based and regenerative platform. This review provides a mechanism-oriented overview of topical haemostatic agents and their clinical applications through a structured classification framework integrated with the physiological basis of coagulation. A narrative review of currently available topical haemostatic agents was performed, classifying agents into five major categories according to material composition, mechanism of action and functional characteristics: mechanical scaffold haemostatic agents, biologically active haemostatic agents, flowable haemostatic agents, sealant and adhesive haemostatic agents and emerging regenerative haemostatic technologies. Mechanical scaffold agents remain foundational tools for routine bleeding control, whereas biologically active and flowable haemostats offer enhanced efficacy in complex bleeding environments. Sealant and adhesive haemostats extend functionality beyond haemostasis towards tissue reinforcement and leakage prevention. Emerging regenerative technologies represent a developing frontier that may integrate bleeding control with tissue repair.
**Keywords:** Topical haemostatic agents, Haemostasis, Surgical bleeding, Coagulation cascad, Surgical sealants

***Received*** 13.07.2026 ***Online published*** 20.07.2026

**Correspondence: Erhan KÜRKÇÜOĞLU**- Eskişehir Osmangazi University, Faculty of Medicine, Medical Student, Eskişehir, Türkiye
e-mail: erhankurkcuoglu33@gmail.com

*Ceylan S, Kürkçüoğlu E , Kandemir T, Topical Haemostatic Agents In Modern Surgery: A Mechanism-Oriented Classification Osmangazi Tıp Dergisi Öğrenci Özel Sayısı, 2026:64-70*

## 1. Introduction

Haemostasis is a highly coordinated physiological process that preserves vascular integrity following tissue injury through interaction among vascular, cellular and plasma-mediated mechanisms. Endothelial disruption elicits an immediate vasoconstrictive response along with platelet adhesion, activation and aggregation, ultimately leading to the formation of a primary platelet plug. This process is subsequently reinforced by activation of the coagulation cascade, resulting in thrombin generation and fibrin clot stabilisation.(1,2)

### Coagulation Cascade

Blood coagulation is a tightly regulated physiological process that prevents excessive bleeding following vascular injury. It involves a series of sequential proteolytic reactions in which inactive plasma zymogens are converted into active serine proteases, forming an enzymatic amplification system that culminates in fibrin clot formation.(1)
Traditionally, the coagulation cascade has been described as three interconnected pathways: the extrinsic, intrinsic and common pathways, all converging on thrombin generation and fibrin formation.(1)

### Extrinsic Pathway

The extrinsic pathway is initiated by vascular injury, which exposes tissue factor (Factor III) expressed on subendothelial cells. Tissue factor binds to circulating Factor VII and the resultant tissue factor–VIIa complex rapidly activates Factor X. This pathway is considered the primary initiator of coagulation *in vivo*.(3)

### Intrinsic Pathway

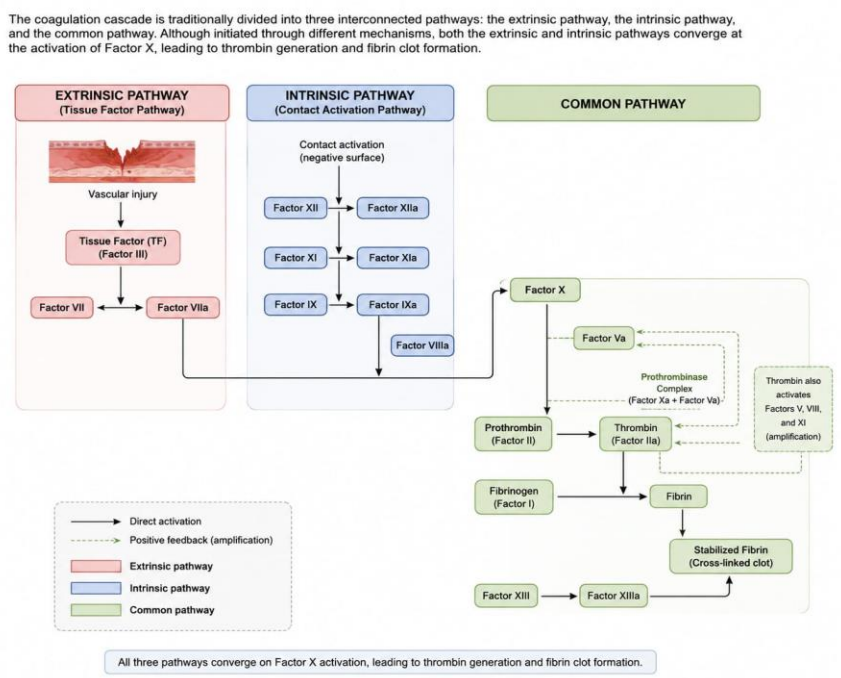
The intrinsic pathway is activated when blood comes into contact with negatively charged surfaces, resulting in the sequential activation of Factors XII, XI and IX. Factor IXa, together with its cofactor Factor VIIIa, activates Factor X. Although historically important, the intrinsic pathway plays a relatively limited role in physiological haemostasis and is mainly reflected in laboratory tests, such as activated partial thromboplastin time. (3)

### Common Pathway

Both pathways converge upon Factor X activation. The subsequent steps include formation of the prothrombinase complex (Factor Xa and Factor Va), conversion of prothrombin (Factor II) to thrombin (Factor IIa) and conversion of fibrinogen (Factor I) to fibrin. Thrombin further amplifies coagulation by activating Factors V, VIII and XI. Finally, Factor XIII stabilises fibrin clots by crosslinking fibrin polymers.(4,5)

### Cell-Based Model of Coagulation

The classical cascade model has been complemented by the cell-based model, which more accurately reflects *in vivo* haemostasis. This model divides coagulation into three overlapping phases: initiation on tissue factor–bearing cells, amplification involving platelet activation and cofactor generation and propagation characterised by a burst of thrombin generation on platelet surfaces. This approach highlights the critical role of cellular components, particularly platelets and endothelial cells.(1)




Despite advances in surgical techniques and perioperative management, intraoperative and post-operative bleeding remain prominent causes of morbidity, prolonged operative time, transfusion requirement and increased healthcare costs. Although conventional surgical techniques such as suturing, ligation, electrocautery and compression remain fundamental components of bleeding control, these methods may be insufficient for diffuse bleeding surfaces, coagulopathic states, minimally accessible operative fields or friable tissues.(6,7)

Consequently, topical haemostatic agents have become increasingly important adjuncts in modern surgery. Over recent decades, these agents have evolved considerably from simple passive biomaterials to sophisticated biologically active, flowable, sealant-based and regenerative technologies. The growing diversity of available haemostatic products has improved the surgeon's ability to tailor bleeding management to the operative environment and bleeding characteristics.(7,8)

Given the expanding range of available topical haemostatic agents and the overlap between their mechanisms and clinical indications, a structured mechanism-oriented classification may facilitate a clearer understanding of their functional properties and surgical applications. In this review, topical haemostatic agents have been grouped into five major categories: mechanical scaffold haemostatic agents, biologically active haemostatic agents, flowable haemostatic agents, sealant and adhesive haemostatic agents and emerging regenerative haemostatic technologies.

## Part I: Mechanical Scaffold Haemostatic Agents

Mechanical scaffold haemostatic agents constitute one of the earliest and most widely used classes of topical haemostatic agents. Rather than directly activating the coagulation cascade, these agents primarily function through physical tamponade, provision of a matrix for platelet adhesion and promotion of intrinsic clot formation. Their efficacy largely depends on interactions between the biomaterial scaffold and native host haemostatic mechanisms.(6,7) Based on biomaterial composition, this group may be further categorised into oxidised cellulose–based, gelatin-based, collagen-based and polysaccharide-based haemostats.(6,7)

### 1.1 Oxidised Cellulose–Based

Oxidised regenerated cellulose–based agents, represented by the Surgicel family, provide a fibrous scaffold facilitating clot formation while generating an acidic microenvironment

that may contribute to bactericidal activity and haemostatic support.(8,9) Variants including Surgicel Original, Fibrillar, Nu-Knit and Snow differ in structural properties and handling characteristics.(8,9)

### 1.2 Gelatin-Based

Gelatin-based agents, such as Gelfoam and Surgifoam, promote haemostasis through absorptive expansion, tamponade and clot stabilisation within their porous matrix.(10)

### 1.3 Collagen-Based

Collagen-derived haemostats, such as Avitene and Helistat, may augment haemostasis by promoting platelet adhesion and aggregation and providing a structural scaffold.(6)

### 1.4 Polysaccharide-Based

Microporous polysaccharide hemospheres such as Arista AH act by rapidly dehydrating blood at the bleeding surface, thereby concentrating endogenous platelets and coagulation proteins to accelerate clot formation.(6)

### 1.5 Clinical Applications of Mechanical Scaffold Haemostatic Agents

Mechanical scaffold haemostats are widely used for low-pressure diffuse bleeding, capillary oozing and raw surgical surfaces and as adjuncts in neurosurgical, abdominal and orthopaedic procedures.(6,7) Their conformability, ease of use and broad availability continue to make them foundational tools in operative haemostasis.(6,7)

## Part II: Biologically Active Haemostatic Agents

Unlike passive mechanical agents, biologically active haemostats directly participate in the coagulation cascade by supplying exogenous clotting factors or enzymatically accelerating fibrin formation. These agents are particularly valuable in diffuse bleeding, coagulopathic states and surgical fields where mechanical haemostasis alone may be insufficient.(6,7) Biologically active haemostats can be broadly categorised into thrombin-based agents and fibrin sealants.(6,7)

### 2.1 Thrombin-Based Agents

Topical thrombin preparations promote haemostasis by converting fibrinogen to fibrin at the bleeding surface, thereby accelerating clot formation independent of upstream coagulation activation.(11,12) Available formulations include bovine-derived, human plasma–derived and recombinant thrombin products, such as Recothrom and Evithrom.(11,12)

### 2.2 Fibrin Sealants

Fibrin sealants replicate the terminal phase of coagulation through a combination of fibrinogen and thrombin, producing a stable fibrin clot at the application site.(5) In addition to haemostasis, these agents may contribute to tissue sealing and reinforcement. Representative agents include Tisseel, Evicel and fibrin sealant patches, such as TachoSil.(8,13)

### 2.3 Fibrin Patch/Advanced Factor-Containing Haemostatic Agents

Advanced biologically active haemostats integrate coagulation factors into matrix-supported delivery systems, improving localisation and persistence of haemostatic activity. Products such as Evarrest and TachoSil capture this evolution from liquid sealants towards structured factor-containing patches.(14)

### 2.4 Clinical Applications of Biologically Active Haemostatic Agents

Biologically active haemostats are particularly useful in diffuse surgical bleeding, coagulopathies, vascular suture-line bleeding, hepatic resection and operative fields where passive haemostats alone may be insufficient.(6,7) Their combined haemostatic and sealing properties have broadened their role across multiple surgical specialties.(6,7)

## Part III: Flowable Haemostatic Agents

Flowable haemostatic agents combine a mechanical matrix with biologically active components in a malleable formulation that can conform to irregular wound geometries.(20,21) By integrating tamponade, scaffold formation and active coagulation support, these agents are particularly effective in diffuse oozing, deep cavities and difficult-to-access bleeding surfaces.(6,15)

### 3.1 Gelatin–Thrombin Flowable Haemostatic Agents

Gelatin–thrombin flowable agents consist of absorbable gelatin matrices combined with topical thrombin, allowing simultaneous mechanical tamponade and accelerated fibrin generation.(16,17) These properties make them particularly useful for controlling bleeding in irregular surgical cavities and raw tissue surfaces.(16,17)

### 3.2 Matrix-Supported Flowable Haemodynamic Agents

More advanced flowable systems incorporate matrix-supported delivery platforms designed to enhance retention at the bleeding site and prolong haemostatic activity. These systems may offer advantages in complex operative bleeding where conventional passive agents may be inadequate.(6,18,19)

### 3.3 Clinical Applications of Flowable Haemodynamic Agents

Flowable haemostats have become increasingly valuable in surgical settings requiring conformability, precise delivery and haemostasis in anatomically challenging spaces. Their utility has been particularly recognised in neurosurgery, cardiovascular surgery and minimally invasive procedures.(6,15)

## Part IV: Sealant And Adhesive Haemostatic Agents

Sealant and adhesive haemostatic agents differ from conventional haemostats in that their principal function extends beyond haemorrhage control to include tissue sealing, reinforcement and prevention of fluid leakage.(7,20) In addition to supporting haemostasis, these agents may facilitate closure of tissue planes and are particularly valuable in neurosurgical, vascular and visceral procedures. Sealant and adhesive haemostatic agents can be broadly categorised into synthetic sealants and adhesive haemostatic patches.(7,20)

### 4.1 Synthetic Sealants

Synthetic sealants form polymerised barriers that reinforce tissues and prevent fluid leakage while contributing to adjunctive haemostasis. Polyethylene glycol–based sealants such as DuraSeal and CoSeal are widely used, particularly in dural closure and vascular surgery.(21,22)

### 4.2 Adhesive Haemostatic Patches

Adhesive haemostatic patches combine tissue adherence with adjunctive haemostatic support, allowing simultaneous bleeding control and tissue sealing. These agents may be particularly useful in fragile tissues and difficult-to-access surgical fields.(8,20,23)

### 4.3 Clinical Applications of Surgical Sealants

Unlike conventional topical haemostats, sealants are often selected not solely for bleeding control but also for preventing cerebrospinal fluid leakage, air leaks, biliary leakage and vascular suture-line bleeding.(7,20) This dual functional role distinguishes them as a unique class within topical haemostatic technologies.(7,20)

## Part V: Emerging Regenerative Haemostatic Technologies

Emerging regenerative haemostatic technologies represent a new generation of topical agents designed not only to control bleeding but also to promote tissue integration, wound healing and biomimetic interactions at the injury site.(6,24) Unlike conventional haemostats that primarily provide passive support or coagulation

enhancement, these agents increasingly incorporate regenerative, biointeractive and engineered material properties.(6,24)

### 5.1 Chitosan-Based Haemostatic Agents

Chitosan-based haemostats promote bleeding control through mucoadhesion, erythrocyte aggregation, platelet interaction and intrinsic antimicrobial activity, while also demonstrating regenerative potential.(25,26)

### 5.2 Self-Assembling Peptide Haemostatic Agents

Self-assembling peptide systems form nanofibre scaffolds upon contact with physiological fluids, creating biomimetic barriers that facilitate both haemostasis and tissue healing.(27)

### 5.3 Biometic and Nanostructured Haemostatic Platforms

Emerging biomimetic materials and nanostructured systems replicate physiological clot architecture while providing enhanced adhesion, responsiveness and regenerative support.(24,28) These next-generation platforms remain largely investigational but represent a promising frontier in surgical haemostasis.(24,28)
Representative technologies:
*Nanofibre haemostatic scaffolds
*Injectable peptide hydrogels
*Smart bioresponsive haemostatic materials

### 5.4 Clinical Applications of Emerging Regenerative Haemostatic Technologies

Regenerative haemostatic technologies are increasingly explored in trauma surgery, endoscopic intervention, neurosurgery and wound repair settings where conventional haemostasis may benefit from simultaneous tissue restoration.(27,28) Their potential dual role in bleeding control and regenerative support distinguishes them from traditional topical haemostatic agents.(6,24)

## 5. Conclusion

Topical haemostatic agents have evolved from conventional passive materials to increasingly sophisticated biologically active, flowable, sealant-based and regenerative technologies. Given the expanding diversity of available agents, a mechanism-oriented classification may facilitate a clearer understanding of their composition, function and clinical applications. This review discussed five major categories of haemostatic agents: mechanical scaffold haemostatic agents, biologically active haemostatic agents, flowable haemostatic agents, sealant and adhesive haemostatic agents and emerging regenerative haemostatic technologies.
Each category possesses distinct advantages, limitations and procedure-specific indications. Mechanical scaffold agents remain fundamental for routine surgical bleeding control, whereas biologically active and flowable agents offer enhanced efficacy in more challenging haemorrhagic settings. Sealant and adhesive technologies have expanded the role of topical haemostats beyond bleeding control towards tissue reinforcement and leakage prevention, while regenerative haemostatic platforms represent a promising frontier for integrating haemostasis with tissue repair.
As surgical practice moves towards increasingly precise and tailored bleeding management, appropriate haemostatic agent selection should be guided by bleeding characteristics, operative environment, biomaterial properties and clinical objectives. Continued comparative studies and technological innovation will further refine the roles of these agents in modern surgery.

***Acknowledgements***

*Preparation for publication of this article is partly supported by Turkish Neurosurgical Society*

## REFERENCES


1. Hoffman M, Monroe DM. Rethinking the coagulation cascade. Curr Hematol Rep. 2005;4(5):391–396.
2. Gale AJ. Current understanding of hemostasis. Toxicol Pathol. 2011;39(1):273-280.
3. Smith SA, Travers RJ, Morrissey JH. How it all starts: initiation of the clotting cascade. Crit Rev Biochem Mol Biol. 2015;50(4):326–336
4. Davie EW, Fujikawa K, Kisiel W. The coagulation cascade: initiation, maintenance, and regulation. Biochemistry. 1991;30(43):10363–10370.
5. Mann KG. Thrombin formation. Chest. 2003;124(3 Suppl):4S–10S.
6. Achneck HE, Sileshi B, Jamiolkowski RM, Albala DM, Shapiro ML, Lawson JH. A comprehensive review of topical hemostatic agents: efficacy and recommendations for use. Ann Surg. 2010;251(2):217-228.
7. Franchini M, Mengoli C, Cruciani M, Bonfanti C, Mannucci PM. A systematic review on the use of topical hemostats in trauma and emergency surgery. BMC Surg. 2018;18(1):68.
8. Genyk Y, Kato T, Pomposelli JJ, Wright JK, Sher LS, Tetens V, et al. Fibrin sealant patch versus oxidized regenerated cellulose for secondary hemostasis after hepatic resection: a randomized controlled trial. J Am Coll Surg. 2016;222(4):485-493.
9. Lewis KM, Spazierer D, Urban MD, Lin L, Redl H, Goppelt A. Comparison of regenerated and non-regenerated oxidized cellulose hemostatic agents. Eur Surg. 2013;45(4):213-220.
10. Lewis KM, Atlee HD, Mannone AJ, Lin L, Goppelt A. Comparison of two gelatin hemostatic matrices in a porcine liver injury model. J Invest Surg. 2013;26(3):141-149.
11. Weber CF, et al. A randomized comparison of recombinant human thrombin and bovine thrombin as adjuncts to hemostasis. J Thorac Cardiovasc Surg. 2008;135(3):514-521.
12. Chapman WC, et al. A phase 3 comparison of plasma-derived human thrombin and bovine thrombin in surgical hemostasis. J Am Coll Surg. 2009;208(2):256-265.
13. Bruckner BA, et al. Fibrin sealant reduces blood loss after cardiac surgery. Ann Thorac Surg. 2006;81(5):1518-1525.
14. Oz MC, et al. Evaluation of a fibrin sealant patch in controlling soft tissue bleeding. J Am Coll Surg. 2012;215(5):638-648.
15. Spotnitz WD. Hemostats, sealants, and adhesives: components of the surgical toolbox. Transfusion. 2012;52 Suppl 1:150S-155S.
16. Nasso G, Piancone F, Bonifazi R, et al. Prospective randomized clinical trial of FloSeal in cardiac surgery. Ann Thorac Surg. 2009;88(5):1520-1526.
17. Tobias JD. Use of Surgiflo hemostatic matrix in surgical bleeding control. J Long Term Eff Med Implants. 2011;21(1):1-12.
18. Fischer L, Seiler CM, Broelsch CE, et al. Hemostatic efficacy of a fibrin pad in severe soft tissue bleeding. Arch Surg. 2011;146(5):559-566.
19. Atallah F, McCalla S, Karakash S, Minkoff H. Please put on your own oxygen mask before assisting others: a call to arms to battle burnout. Am J Obstet Gynecol. 2016 Dec;215(6):731.e1-731.e6.
20. Kim KD, Wright NM. Polyethylene glycol hydrogel dural sealant in neurosurgery. Spine. 2009;34(18):1909-1915.
21. Miller JS, et al. Clinical evaluation of CoSeal surgical sealant in vascular reconstruction. J Vasc Surg. 2006;44(5):1002-1011.
22. Champagne PO, Lemoine E, Bojanowski MW. Surgical management of giant sphenoid wing meningiomas encasing major cerebral arteries. Neurosurg Focus. 2018 Apr;44(4):E12.
23. Lewis KM, et al. Hemopatch as a novel sealing hemostatic patch: clinical appraisal. Med Devices (Auckl). 2014;7:1-10.
24. Cheng Y, et al. Application and outlook of topical hemostatic materials: a comprehensive review. Bioact Mater. 2021;6(11):3826-3851.
25. Wedmore I, et al. A special report on the chitosan-based hemostatic dressing for combat casualty care. J Trauma. 2006;60(3):655-658.
26. Xi J, Long M, Tang L, Wang D, Shuai Z. First-principles prediction of charge mobility in carbon and organic nanomaterials. Nanoscale. 2012 Aug 7;4(15):4348-69.
27. Sansotta N, Alessio MG, Norsa L, Previtali G, Ferrari A, Guerra G, D'Antiga L. Trend of Antitissue Transglutaminase Antibody Normalization in Children With Celiac Disease Started on Gluten-free Diet: A Comparative Study Between Chemiluminescence and ELISA Serum Assays. J Pediatr Gastroenterol Nutr. 2020 Jan;70(1):37-41.
28. Tebala GD, Hameed W, Di Saverio S, Gallo G, Bond-Smith G. Proposal and Validation of a New Classification of Surgical Outcomes after Colorectal Resections within an Enhanced Recovery Programme. Surg Res Pract. 2021 May 11;2021:8864555.