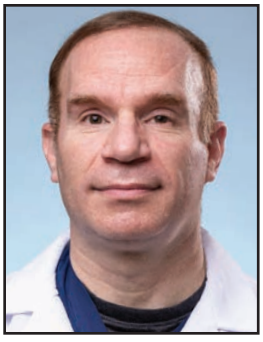
Douglas G. Adler MD, FACG, AGAF, FASGE, Series Editor

Topical Endoscopic Hemostatic Agents for Gastrointestinal Bleeding

Magnus Chun



Douglas G. Adler

BACKGROUND

Gastrointestinal bleeding (GIB) is associated with significant morbidity and mortality. Despite improved endoscopic practices for GIB, approximately 8-15% of patients fail primary endoscopic therapy, which includes injection, thermal, and mechanical therapy.[1] These techniques require precise localization of the bleeding source and may not be as effective in patients with lesions that are difficult to access, have tumor-associated bleeding, or broad based bleeding sources.[2] Additionally, a high level of endoscopic expertise is required for these modalities which may not be available at smaller hospitals.

Recently, topical endoscopic hemostatic agents were introduced to treat GIB.[3] These agents have had promising results as salvage therapy or even as primary therapy without requiring precise localization or extensive technical expertise.[3,4] There are five approved agents (Table 1): hemostatic agent TC-325 (Hemospray™, Cook Medical Inc, Winston-Salem, North Carolina, US), synthetic self-assembling peptide agent (PuraStat™, 3D-Matrix, Europe Ltd., France), Endoclot™ (Endoclot Plus Inc., Santa Clara, California, US) polysaccharide hemostatic system (PHS), biocompatible natural polymer UI-EWD (Nexpowder™, NextBiomedical Co., Incheon, South Korea) and erythrocyte protein network (Ankaferd Blood Stopper™, ABS, Ankaferd Health Products Ltd., Turkey).[5]

Topical endoscopic hemostatic agents are intended to control active non-variceal GIB (NVGIB) by delivering a substance over the bleeding site through a catheter via the endoscope working channel. The main advantage of topical agents is that less precision is required when applying the agent to the bleeding site. This allows for treatment of lesions that may be difficult to

Magnus Chun MD[1] Douglas G. Adler MD, FACG, AGAF, FASGE[2] [1]Department of Internal Medicine, University of Nevada, Las Vegas, NV [2]Center for Advanced Therapeutic Endoscopy (CATE), Porter Advent Hospital, Denver, CO

Table 1. Summary of Topical Endoscopic Hemostatic Agents

Agent/Trade Name	Composition	Mechanism of Action	Approved Application
TC-325 (Hemospray™)	Granular mineral-based	Absorbs water and activates the clotting cascade to form a mechanical tamponade	Peptic ulcer disease, variceal GIB, lower GIB, tumor bleeding
PuraStat™	Synthetic self-assembling peptide agent	Peptide solution forms a 3-dimensional nano-fiber hydrogel scaffold of beta-sheets	Bleeding secondary to therapeutic endoscopic procedures
Endoclot™	Absorbable starch-based modified polysaccharide	Absorbs water and concentrates platelets and clotting factors to create a mechanical tamponade	Peptic ulcer disease, malignant tumors, esophageal ulcers, esophagitis, post-interventional bleeding
UI-EWD (Nexpowder™)	Biocompatible natural polymer	Forms adhesive hydrogel in presence of water	Prophylaxis post-intervention, Peptic ulcer disease, malignant tumors, and post-interventional bleeding
Ankaferd Blood Stopper™	Erythrocyte protein network	Encapsulated protein network provides focal points for erythrocyte aggregation	Only approved in Turkey: non-variceal upper GIB (Case reports: peptic ulcer disease, malignant GIB, esophageal variceal bleeding and post-polypectomy bleeding)

access or refractory to standard therapy.[6] Although recent studies have shown that hemostatic agents were effective in NVGIB, there had been reports of high re-bleeding rates.[5] Topical agents can also be used prophylactically to reduce the risk of bleeding following polypectomy, endoscopic mucosal resection (EMR), or endoscopic submucosal dissection (ESD). These agents can also be used to treat or reduce the risk of sphincterotomy bleeding during endoscopic retrograde cholangiopancreatography (ERCP).

This manuscript aims to discuss the efficacy, safety, advantages, and disadvantages of the FDA-approved topical endoscopic hemostatic agents.

Hemostatic agent TC-325/Hemospray

Hemostatic agent TC-325 is a metabolically inert, nontoxic, granular mineral-based inorganic powder that when in contact with blood will induce hemostasis by absorbing water and activating the clotting cascade. As a result, a mechanical tamponade and adhesive barrier form over the bleeding site.[7] Hemospray is deployed through the endoscope-integrated catheter in short bursts when a compressed carbon dioxide propellant is activated by the device's trigger.

Hemospray has been shown to be successful in controlling bleeding from peptic ulcer disease, variceal GIB, and lower GIB as both monotherapy and as an adjunctive therapy to conventional therapy.[8,9,10,11] (Figures 1 and 2) Sung et al. and Kwek et al. reported hemostasis in 90% of patients with monotherapy and 100% of patients as an adjunctive therapy.[8,9] In another study, Ibrahim et al. reported 100% hemostasis in nine patients treated with monotherapy.[10] In regards to lower GIB, Hemospray was effective in achieving hemostasis for spurting post-polypectomy bleeding that did not respond to clipping.[11] Additionally, in a systematic review and meta-analysis by Facciorusso et al., the immediate hemostasis rate for Hemospray monotherapy in 8 studies with 175 patients was 96.2% (95% CI 93.5-99.7%).[12] Bleeding from gastrointestinal tumor may sometimes be diffuse and lack a specific target suitable for endoscopic hemostasis. In these cases, Hemospray is a good option to provide short-term hemostasis. In a large multicenter study conducted by Pittayanon et al.,

they found that hemostasis was achieved with Hemospray in 98% of cases.[13]

However, the downside of Hemospray monotherapy is that studies show high rebleeding rates at 7 days typically ranging between 15-49%.[12,14,15,16] Facciorusso et al. found that there was a 9.8% (95% CI 3.8-15.8%) pooled 7-day rebleeding rate and a 12.3% (95% CI 6.0-18.7%) pooled 30-day rebleeding rate. A study by Cahyadi et al. found even higher rebleeding rates at 3 days (43.1%) and at 7 days (49.0%).[17] This is likely due to the fact that while Hemospray induces coagulation, it generally does not treat the underlying cause of a bleed. Recent guidelines published in the Annals of Internal Medicine recommend that Hemospray be used only as a temporizing measure when primary endoscopy therapy fails and should not be used as a monotherapy due to the high re-bleeding rates.[18]

Hemospray can often limit endoscopic visualization after deployment, and when it is used before other hemostatic agents, there may be a risk of obscuring the boundaries of a lesion (making it more difficult to implement other hemostatic options if they are needed).[19] As Hemospray is sprayed, the cloud of powder can temporarily fill the endoscopic field of view and if the endoscope's tip is too close to the site of application, the powder can adhere directly to the lens. To avoid this, we recommend releasing the powder in short 1- to 2-second bursts and maintaining the endoscope's tip at least 1-2 cm away from the lesion.

PuraStat

PuraStat is a biocompatible synthetic peptide gel consisting of a repeating sequence of the amino acids Arginine, Alanine, and Aspartic Acid. Once Purastat gel comes in contact with blood, the peptide solution is neutralized to form a 3-dimensional nano-fiber hydrogel scaffold of beta-sheets. This structure, similar to the extracellular matrix, forms a physical barrier over the bleeding vessel or bleeding site to achieve hemostasis.[20]

PuraStat is currently intended for prophylaxis of bleeding secondary to therapeutic endoscopic procedures such as endoscopic submucosal dissection (ESD) or endoscopic mucosal resection (EMR), although it has been used in a wide variety of contexts. (Figures 3 and 4) Prior studies have shown that post-ESD, there was a smaller mean number of any secondary temporizing measures required when PuraStat was used initially compared to the control group without PuraStat (1.0±1.4 vs 4.9±5.2, $p<0.001$), demonstrating the efficacy of PuraStat in managing intraoperative bleeding. [21,22] In a study by Uraoka et al., only 1 out of 51 included patients had post-ESD bleeding after being treated with PuraStat.[23] However, Gomi et al. 2024, in a more recent and larger study of 101 patients, did not find that PuraStat was associated with improved rates of post-ESD bleeding, highlighting the need for further research in this area.

The efficacy of PuraStat in managing post-sphincterotomy bleeds has also been studied. Ogura

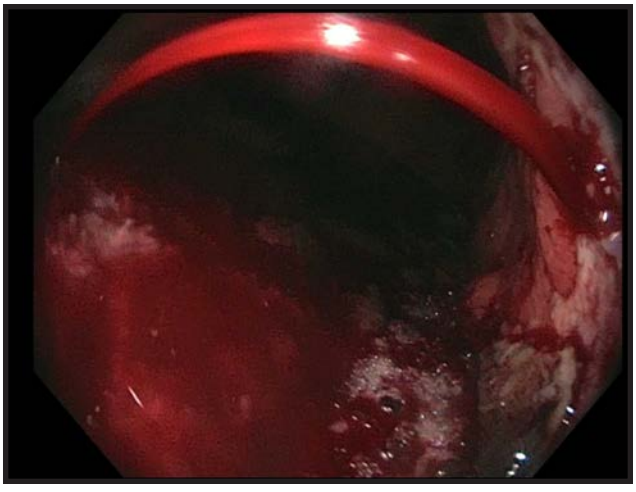


Figure 1a. Gastric variceal bleed with very brisk jet of blood seen in the gastric cardia

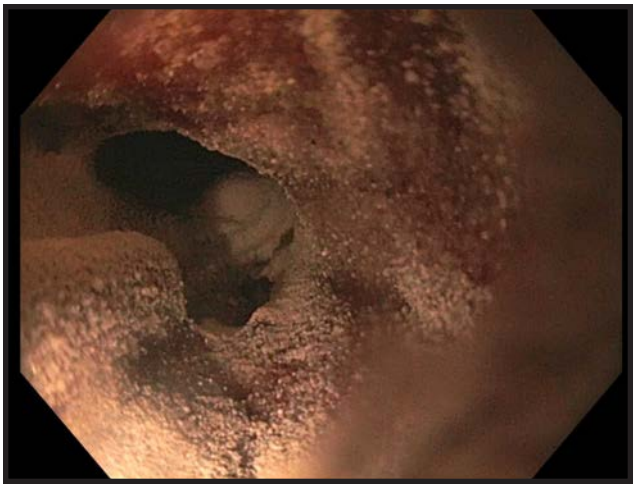


Figure 1b. Same site after application of Hemospray. Note that bleeding has stopped but visualization is limited.

et al. found that 98% of patients achieved complete cessation of bleeding with PuraStat monotherapy.[24] Kishore et al. found that 96.5% (95% CI: 92.3-100) of patients achieved complete cessation of bleeding with PuraStat monotherapy, with a rebleeding rate of 3.10% (95% CI: 0.50-5.60).[25]

Furthermore, in a recent meta-analysis, three studies showed PuraStat to be effective in both primary and rescue hemostasis for bleeds caused by peptic ulcer disease, large polyps, tumors, and capillary lesions. [20,26,27,28] For primary hemostasis, the pooled immediate hemostasis rate was 87% (95% CI 75%-94%) and the pooled rebleeding rate within 30 days was 10% (95% CI: 6%-16%).[20,26,27,28] In Bianchi et al.'s study, 111 patients were included with an initial hemostatic success rate of 94% (95% CI 88-99%). When used as a secondary hemostatic product, PuraStat had a hemostatic success rate of 75% (95% CI 59-91%). The rebleeding rates at 3 and 7 days were 9% and 15% after primary use and 13% and 19% after secondary use, respectively. The overall rebleeding rate at 30 days was 16%.[20]

In comparison with Hemospray, PuraStat is a transparent hemostatic agent that does not compromise endoscopic visualization after deployment. This makes it possible to check post-therapy bleeding status and continue further interventions, if needed. It is already prepared for the endoscopist in a single prefilled, ready-to-use syringe and deployed through the endoscopic catheter. Given that PuraStat is a gel, it is also highly versatile and can be used in narrow spaces where the bleeding site is difficult to reach with a hemoclip or a thermal probe.

However, similar to Hemospray, the downside of PuraStat is it has a high rebleeding rate of 10%-15% at 7 days if used as monotherapy.[20, 26] This is a drawback of hemostatic agents in general given they can only bind to sites with active bleeding for 12-24 hours.[29] However, one recent retrospective study showed there was no statistical significant differences in rebleeding (p=0.64) or mortality (p=0.69) when comparing initial PuraStat use and the standard care (i.e. injection, hemoclips, etc.).[30]

Endoclot

Endoclot is a starch-derived compound consisting of biocompatible absorbable hemostatic polysaccharide that when in contact with blood, will rapidly absorb water. This causes a high concentration of clotting factors, red blood cells, and platelets to accumulate at the bleeding site accelerating the hemostasis process.[3] Afterwards, the polysaccharide will form a gelled, adhesive matrix providing a mechanical barrier to seal and potentially protect the wound site from further bleeding.[31]

Endoclot is indicated as either monotherapy or rescue therapy for both upper and lower GIB, with studies showing efficacy in hemostasis for peptic ulcer disease, malignant tumors, esophageal ulcers and esophagitis, as well as post-interventional

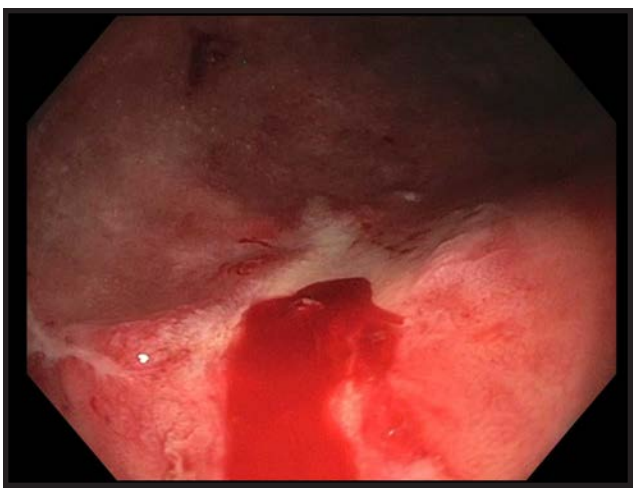


Figure 2a. Gastric ulcer with visible vessel and brisk bleeding

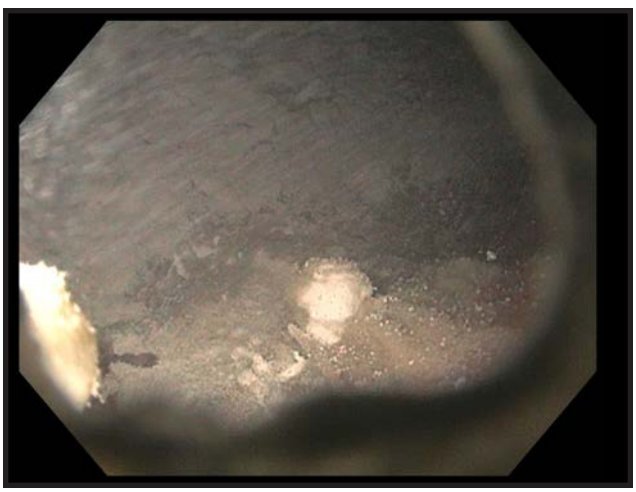


Figure 2b. Same lesion after application bipolar electrocautery and application of Hemospray with hemostasis achieved

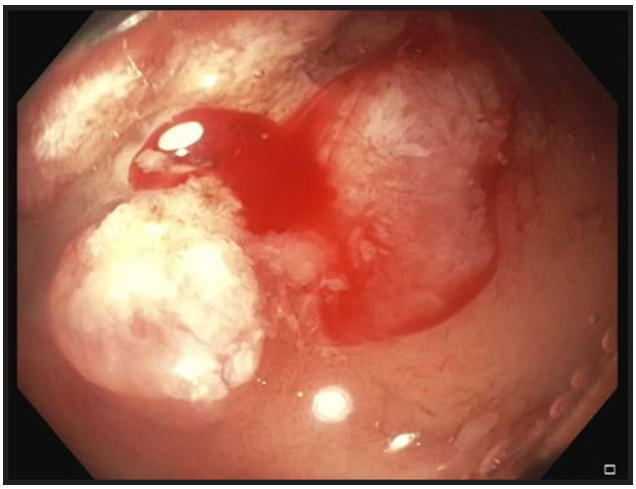


Figure 3a. Actively bleeding duodenal ulcer

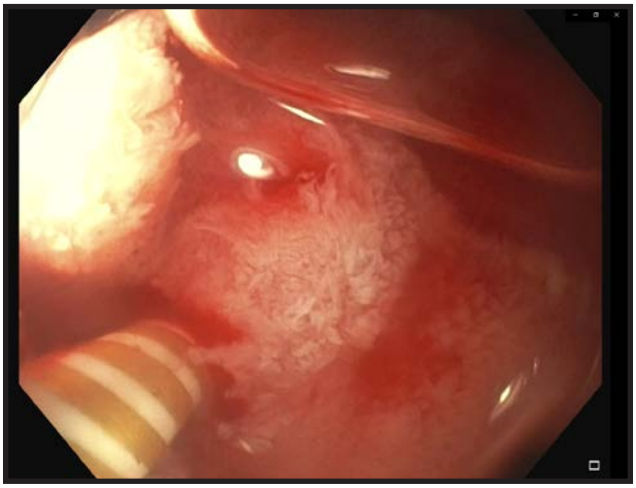


Figure 3b. Bipolar electrocautery applied to the ulcer

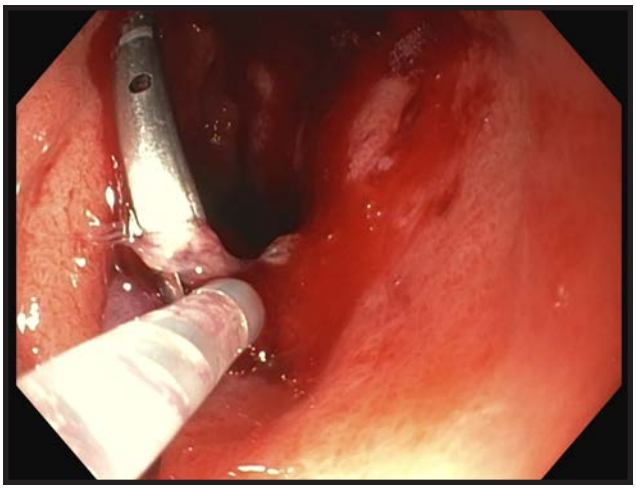


Figure 4. Application of Purastat to a duodenal ulcer after placement of an endoscopic clip. Residual bleedings stopped after Purasat application.

bleeding.[32,33,34,35,36] In a recent meta-analysis of 5 studies and 398 patients, the immediate hemostasis rate for any GIB after Endoclot monotherapy was 86% (95% CI: 80%-90%), with a rebleeding risk within 30 days of 10% (95% CI 6%-16%).[26] In a recent multicenter analysis of 43 patients by Hagel et al., the immediate hemostasis rate was 81.8% when Endoclot was used as a salvage therapy. In one study, among patients with tumor bleeding, there was a 0% rebleeding rate after treatment with Endoclot as monotherapy.[35]

Furthermore, Endoclot is delivered differently compared to other hemostatic agents. Hemospray is delivered at high pressure with a carbon dioxide cartridge which can be advantageous in situations with high pressure bleeding. However, the high-pressure application from the carbon dioxide can potentially cause tissue injury as well. Two studies have shown perforation in their patient cohort after Hemospray application due to high-pressure carbon dioxide application.[35,37] In contrast, the pressure at which Endoclot is sprayed is much lower making it more suitable for localized bleeding lesions and has lower risks of causing tissue injury.[38]

The main disadvantage of Endoclot, similarly to other hemostatic agents, is the risk of rebleeding due to low binding times of the adhesive matrix to the bleeding site. Limited studies report the advantages and disadvantages of Endoclot compared to other forms of hemostatic agents. Beg et al. reported on the use of Endoclot by novice operators. In their study, assisting nurses who had no specific training using Endoclot had success and ease of use when it was applied.[32]

Nexpowder

Nexpowder is a biocompatible natural polymer composed of oxidized dextran and succinic anhydride that gets converted to adhesive hydrogel when in contact with water. It then forms a mechanical barrier at bleeding site(s) to promote hemostasis.[39] It is deployed by insoluble air propellant and uses a pre-installed battery as its power source, allowing air pressure generated from the air pump in the delivery system's spray body to provide a force to move the powder into the delivery catheter.[39] The advantage of Nexpowder is that it does not require active bleeding to

(continued on page 26)

(continued from page 24)

work which allows it to have a potential role in prophylaxis post-procedural.[39] However, most studies show promising results for Nexpowder as a role in primary hemostasis or prophylaxis post-intervention as well.[40,41,42]

Nexpowder is indicated as either monotherapy or rescue therapy for both upper and lower GIB, with studies showing efficacy in hemostasis for peptic ulcer disease, malignant tumors, and post-interventional bleeding.[40,41,42] It can also be used as prophylaxis post-intervention.[40,42] In a recent meta-analysis of 3 studies and 114 patients, the immediate hemostasis rate for any GIB after Nexpowder monotherapy was 96% (95% CI: 91%-99%), with a rebleeding risk within 30 days of 8% (95% CI 3%-20%).[26] Shin et al. found that there was immediate hemostasis in 100% (n=23) of their patient cohort when using Nexpowder monotherapy for active bleeds secondary to luminal malignant tumors. However, there was a high rate of rebleeding within 1 month in 26.1% and 22.5% of their patients when using Nexpowder as monotherapy and salvage therapy, respectively.[42] All three studies used Nexpowder post-intervention as a prophylaxis for acute bleeding.[40,41,42]

One advantage of Nexpowder is it has a lower rebleeding rate within 30 days (8%) compared to other hemostatic agents (subgroup differences: $p < 0.01$).[26] In a study conducted by Park et al., they found that only 2 out of 54 patients (3.7%) had rebleeding within 30 days after using Nexpowder as a monotherapy.[41] In another study, Park et al. used a second-look endoscopy after 24 hours of applying the Nexpowder as a monotherapy and saw that the hydrogel from Nexpowder was still attached to the bleeding site in 69% of their patients 24 hours later.[40] Shin et al. found that the when using Nexpowder as a monotherapy, the hydrogel was reported to be present at 70.2% of sprayed bleeding sites using second-look endoscopy at 24 hours.[43]

Ankaferd Bloodstopper

Ankaferd Bloodstopper (ABS) is a hemostatic agent only approved in Turkey and Bosnia-Herzegovina and composed of a mixture of plants, including *Thymus vulgaris, Glycrrhiza glabra, Vitis vinifera, Alpinia officinarum,* and *Urtica dioica*. The mechanism of action of ABS is it rapidly forms an encapsulated protein network that provides multiple focal points for erythrocyte and leukocyte aggregation, including fibrinogen, which, in turn, induces protein aggregation.[44,45] ABS is a topical powder application that is sprayed via a catheter through the working channel of the endoscope. ABS is currently approved in Turkey and Bosnia-Herzegovina for upper and lower GIB that is only refractory to conventional hemostatic measures.[3]

There has been a relative paucity of studies analyzing the effectiveness and safety of ABS monotherapy and salvage therapy. No safety concerns have been reported to date. A case series of 27 patients with active, non-variceal GIB showed an immediate hemostasis rate of 73% when ABS was used as a monotherapy and 100% when used in combination with standard therapy.[46] Rebleeding within 48 hours was seen in 15.8% of patients with ABS monotherapy and 33.3% with ABS salvage therapy.[46] There are multiple case reports of the success of immediate hemostasis using ABS monotherapy in patients with peptic ulcer disease, malignant GIB, esophageal variceal bleeding and post-polypectomy bleeding.[47,48,49,50,51,52,53,54]

CONCLUSION

Topical hemostatic agents have been shown to be effective in hemostasis for gastrointestinal bleeding, especially when used in combination with conventional methods or as salvage therapy. Limited studies have demonstrated high primary hemostasis rates in both upper and lower GIB when used as monotherapy but with some risk of rebleeding. Topical hemostatic agents are simple to use and do not require a high level of endoscopic expertise to employ. ■

References

1 Lau JY, Barkun A, Fan DM, Kuipers EJ, Yang YS, Chan FK. Challenges in the management of acute peptic ulcer bleeding. Lancet. 2013 Jun 8;381(9882):2033-43. doi: 10.1016/S0140-6736(13)60596-6. PMID: 23746903.

2 Barkun A, Bardou M, Marshall JK, Nonvariceal Upper GI Bleeding Consensus Conference Group. Consensus recommendations for managing patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med. 2003;139(10):843- 857.

3 Bustamante-Balén M, Plumé G. Role of hemostatic powders in the endoscopic management of gastrointestinal bleeding. World J Gastrointest Pathophysiol. 2014 Aug 15;5(3):284-92. doi: 10.4291/wjgp.v5.i3.284. PMID: 25133029; PMCID: PMC4133526.

4 Barkun AN, Moosavi S, Martel M. Topical hemostatic agents: a systematic review with particular emphasis on endoscopic application in GI bleeding. Gastrointest Endosc 2013; 77: 692–700

5 Chen YI, Barkun AN. Hemostatic powders in gastrointestinal bleeding: A systematic review. Gastrointest Endosc Clin N Am 2015; 25: 535–552

6 Giday SA, Kim Y, Krishnamurty DM, Ducharme R, Liang DB, Shin EJ, Dray X, Hutcheon D, Moskowitz K, Donatelli G, Rueben D, Canto MI, Okolo PI, Kalloo AN. Long-term randomized controlled trial of a novel nanopowder hemostatic agent (TC-325) for control of severe arterial upper gastrointestinal bleeding in a porcine model. Endoscopy 2011; 43: 296-299 [PMID: 21384319 DOI: 10.1055/s-0030-1256125]

7 Ibrahim M, El-Mikkawy A, Mostafa I, Devière J. Endoscopic treatment of acute variceal hemorrhage by using hemostatic powder TC-325: a prospective pilot study. Gastrointest Endosc. 2013;78(5):769-773.

8 Sung JJY, Luo D, Wu JCY, et al. Early clinical experience of the safety and effectiveness of Hemospray in achieving hemostasis in patients with acute peptic ulcer bleeding. Endoscopy. 2011;43(4):291-295.

9 Kwek BEA, Ang TL, Ong PLJ, et al. TC-325 versus the conventional combined technique for endoscopic treatment of peptic ulcers with high-risk bleeding stigmata: A randomized pilot study. *J Dig Dis.* 2017; 18(6):323-329

10 Ibrahim M, El-Mikkawy A, Mostafa I, Devière J. Endoscopic treatment of acute variceal hemorrhage by using hemostatic powder TC-325: a prospective pilot study. Gastrointest Endosc. 2013;78(5):769-773.

11 Iveković H, Bilic B, Markos P, Rustemovic N, Ostojic R, Mönkemüller K. Successful use of Hemospray to control refractory post-polypectomy bleeding. Endoscopy. 2015;47:E466-E467

12 Facciorusso A, Bertini M, Bertoni M, Tartaglia N, Pacilli M, Ramai D, Mohan BP, Chandan S, Ambrosi A, Sacco R. Effectiveness of hemostatic powders in lower gastrointestinal bleeding: a systematic review and meta-analysis. Endosc Int Open. 2021 Aug;9(8):E1283-E1290. doi: 10.1055/a-1495-4764. Epub 2021 Jul 16. PMID: 34447877; PMCID: PMC8383089.

13 Pittayanon R, Rerknimitr R, Barkun A. Prognostic factors affecting outcomes in patients with malignant GI bleeding treated with a novel endoscopically delivered hemostatic powder. Gastrointest Endosc. 2018;87(4):994-1002

14 Smith LA, Stanley AJ, Bergman JJ, et al. Hemospray application in nonvariceal upper gastrointestinal bleeding: results of the Survey to Evaluate the Application of Hemospray in the Luminal Tract. J Clin Gastroenterol. 2014;48(10):e89-92.

15 Cahyadi O, Bauder M, Meier B, Caca K, Schmidt A. Effectiveness of TC-325 (Hemospray) for treatment of diffuse or refractory upper gastrointestinal bleeding – a single center experience. Endosc Int Open. 2017;5(11):E1159-E1164

16 Sinha R, Lockman KA, Church NI, Plevris JN, Hayes PC. The use of hemostatic spray as an adjunct to conventional hemostatic measures in high-risk nonvariceal upper GI bleeding (with video). Gastrointest Endosc. 2016;84(6):900-906.e3.

17 Cahyadi O, Bauder M, Meier B, Caca K, Schmidt A. Effectiveness of TC-325 (Hemospray) for treatment of diffuse or refractory upper gastrointestinal bleeding - a single center experience. Endosc Int Open. 2017 Nov;5(11):E1159-E1164. doi: 10.1055/s-0043-118794. Epub 2017 Nov 8. PMID: 29124127; PMCID: PMC5677459.

18 Barkun AN, Almadi M, Kuipers EJ et al. Management of nonvariceal upper gastrointestinal bleeding: guideline recommendations from the International Consensus Group. Ann Intern Med 2019; 171: 805–822

19 Barkun AN, Moosavi S, Martel M. Topical hemostatic agents: a systematic review with particular emphasis on endoscopic application in GI bleeding. Gastrointest Endosc. 2013;77(5):692-700.

20 Branchi F, Klingenberg-Noftz R, Friedrich K, Bürgel N, Daum S, Buchkremer J, Sonnenberg E, Schumann M, Treese C, Tröger H, Lissner D, Epple HJ, Siegmund B, Stroux A, Adler A, Veltzke-Schlieker W, Autenrieth D, Leonhardt S, Fischer A, Jürgensen C, Pape UF, Wiedenmann B, Möschler O, Schreiner M, Strowski MZ, Hempel V, Huber Y, Neumann H, Bojarski C. PuraStat in gastrointestinal bleeding: results of a prospective multicentre observational pilot study. Surg Endosc. 2022 May;36(5):2954-2961. doi: 10.1007/s00464-021-08589-6. Epub 2021 Jun 15. PMID: 34129089; PMCID: PMC9001238.

21 Subramaniam S, Kandiah K, Chedgy F, Fogg C, Thayalasekaran S, Alkandari A, Baker-Moffatt M, Dash J, Lyons-Amos M, Longcroft-Wheaton G, Brown J, Bhandari P. A novel self-assembling peptide for hemostasis during endoscopic submucosal dissection: a randomized controlled trial. Endoscopy. 2021;53:27–35. doi: 10.1055/a-1198-0558.

22 Uraoka T, Uedo N, Oyama T, Saito Y, Yahagi N, Fujimoto A, Kawahara Y, Mabe K, Hikichi T, Yamamoto Y, Tajiri H. Efficacy and Safety of a Novel Hemostatic Peptide Solution During Endoscopic Submucosal Dissection: A Multicenter Randomized Controlled Trial. Am J Gastroenterol. 2023;118:276–283. doi: 10.14309/ajg.0000000000002060.

23 Uraoka T, Ochiai Y, Fujimoto A, Goto O, Kawahara Y, Kobayashi N, Kanai T, Matsuda S, Kitagawa Y, Yahagi N. A novel fully synthetic and self-assembled peptide solution for endoscopic submucosal dissection-induced ulcer in the stomach. Gastrointest Endosc. 2016 Jun;83(6):1259-64. doi: 10.1016/j.gie.2015.11.015. Epub 2015 Dec 1. PMID: 26608126.

24 Takeshi Ogura, Saori Ueno, Atsushi Okuda, Nobu Nishioka, Masanori Yamada, Masahiro Yamamura, Nobuhiro Hattori, Junichi Nakamura, Kimi Bessho, Hiroki Nishikawa, Step-Up Strategy for Endoscopic Hemostasis Using PuraStat After Endoscopic Sphincterotomy Bleeding (STOP Trial), Techniques and Innovations in Gastrointestinal Endoscopy, Volume 26, Issue 3, 2024, Pages 224-229, ISSN 2590-0307, https://doi.org/10.1016/j.tige.2024.03.005. (https://www.sciencedirect.com/science/article/pii/S2590030724000199)

25 Kishore, Mehwish MD,*; Khan, Zarak H. MD; Puli, Srinivas MD. S132 Meta-Analysis and Systematic Review of the Emerging use of PuraStat as Hemostatic Agent for Post-Sphincterotomy Bleeding. The American Journal of Gastroenterology 119(10S):p S99, October 2024. | DOI: 10.14309/01.ajg.0001028896.06269.e4

26 Alali AA, Moosavi S, Martel M, Almadi M, Barkun AN. Topical hemostatic agents in the management of upper gastrointestinal bleeding: a meta-analysis. Endosc Int Open. 2023 Apr 24;11(4):E368-E385. doi: 10.1055/a-1984-6895. PMID: 37102185; PMCID: PMC10125779.

27 de Nucci G, Reati R, Arena I, Bezzio C, Devani M, Corte CD, Morganti D, Mandelli ED, Omazzi B, Redaelli D, Saibeni S, Dinelli M, Manes G. Efficacy of a novel self-assembling peptide hemostatic gel as rescue therapy for refractory acute gastrointestinal bleeding. Endoscopy. 2020 Sep;52(9):773-779. doi: 10.1055/a-1145-3412. Epub 2020 Apr 21. PMID: 32316041.

28 Labianca O, Sica M, Zulli C et al. Use of Purastat in management of gastro-intestinal bleeding: out experience. Endoscopy 2021; 53: S97-S98

29 Chen YI, Barkun AN. Hemostatic Powders in Gastrointestinal Bleeding: A Systematic Review. Gastrointest Endosc Clin N Am. 2015 Jul;25(3):535-52. doi: 10.1016/j.giec.2015.02.008. Epub 2015 Apr 18. PMID: 26142037.

30 Ballester R, Costigan C, O'Sullivan AM, Sengupta S, McNamara D. Efficacy and applications for PuraStat® use in the management of unselected gastrointestinal bleeding: A retrospective observational study. World J Gastrointest Endosc. 2025 Mar 16;17(3):98021. doi: 10.4253/wjge.v17.i3.98021. PMID: 40125508; PMCID: PMC11923975.

31 AMP technology. Polymer Solution for hemostasis. 2011. Available from: http: //endoclot.com/technology.html. Last accessed: September 2025

32 Beg S, Al-Bakir I, Bhuva M, Patel J, Fullard M, Leahy A. Early clinical experience of the safety and efficacy of EndoClot in the management of non-variceal upper gastrointestinal bleeding. Endosc Int Open. 2015 Dec;3(6):E605-9. doi: 10.1055/s-0034-1393087. Epub 2015 Nov 27. PMID: 26716120; PMCID: PMC4683139.

33 Kim YJ, Park JC, Kim EH, Shin SK, Lee SK, Lee YC. Hemostatic powder application for control of acute upper gastrointestinal bleed-

ing in patients with gastric malignancy. Endosc Int Open. 2018 Jun;6(6):E700-E705. doi: 10.1055/a-0593-5884. Epub 2018 May 25. PMID: 29868635; PMCID: PMC5979193.

34 Prei JC, Barmeyer C, Bürgel N, Daum S, Epple HJ, Günther U, Maul J, Siegmund B, Schumann M, Tröger H, Stroux A, Adler A, Veltzke-Schlieker W, Jürgensen C, Wentrup R, Wiedenmann B, Binkau J, Hartmann D, Nötzel E, Domagk D, Wacke W, Wahnschaffe U, Bojarski C. EndoClot Polysaccharide Hemostatic System in Nonvariceal Gastrointestinal Bleeding: Results of a Prospective Multicenter Observational Pilot Study. J Clin Gastroenterol. 2016 Nov/Dec;50(10):e95-e100. doi: 10.1097/MCG.0000000000000615. PMID: 27552329.

35 Hagel AF, Raithel M, Hempen P, Preclik G, Dauth W, Neurath MF, Gschossman J, Konturek PC, Albrecht H. Multicenter analysis of endoclot as hemostatic powder in different endoscopic settings of the upper gastrointestinal tract. J Physiol Pharmacol. 2020 Oct;71(5). doi: 10.26402/jpp.2020.5.06. Epub 2021 Jan 16. PMID: 33475093.

36 Park JC, Kim YJ, Kim EH, Lee J, Yang HS, Kim EH, Hahn KY, Shin SK, Lee SK, Lee YC. Effectiveness of the polysaccharide hemostatic powder in non-variceal upper gastrointestinal bleeding: Using propensity score matching. J Gastroenterol Hepatol. 2018 Aug;33(8):1500-1506. doi: 10.1111/jgh.14118. Epub 2018 Mar 5. PMID: 29415371.

37 Yau AH, Ou G, Galorport C, Amar J, Bressler B, Donnellan F, Ko HH, Lam E, Enns RA. Safety and efficacy of Hemospray® in upper gastrointestinal bleeding. Can J Gastroenterol Hepatol. 2014 Feb;28(2):72-6. doi: 10.1155/2014/759436. PMID: 24501723; PMCID: PMC4071892.

38 Vitali F, Naegel A, Atreya R, Zopf S, Neufert C, Siebler J, Neurath MF, Rath T. Comparison of Hemospray® and Endoclot™ for the treatment of gastrointestinal bleeding. World J Gastroenterol. 2019 Apr 7;25(13):1592-1602. doi: 10.3748/wjg.v25.i13.1592. PMID: 30983819; PMCID: PMC6452236.

39 Bang B, Lee E, Maeng J, Kim K, Hwang JH, Hyon SH, Hyon W, Lee DH. Efficacy of a novel endoscopically deliverable muco-adhesive hemostatic powder in an acute gastric bleeding porcine model. PLoS One. 2019 Jun 11;14(6):e0216829. doi: 10.1371/journal.pone.0216829. PMID: 31185029; PMCID: PMC6559629.

40 Park JS, Bang BW, Hong SJ, Lee E, Kwon KS, Kim HK, Shin YW, Lee DH. Efficacy of a novel hemostatic adhesive powder in patients with refractory upper gastrointestinal bleeding: a pilot study. Endoscopy. 2019 May;51(5):458-462. doi: 10.1055/a-0809-5276. Epub 2019 Jan 10. PMID: 30630195.

41 Park JS, Kim HK, Shin YW, Kwon KS, Lee DH. Novel hemostatic adhesive powder for nonvariceal upper gastrointestinal bleeding. Endosc Int Open. 2019 Dec;7(12):E1763-E1767. doi: 10.1055/a-0982-3194. Epub 2019 Dec 10. PMID: 31828214; PMCID: PMC6904239.

42 Shin J, Cha B, Park JS, Ko W, Kwon KS, Lee JW, Kim HK, Shin YW. Efficacy of a novel hemostatic adhesive powder in patients with upper gastrointestinal tumor bleeding. BMC Gastroenterol. 2021 Jan 28;21(1):40. doi: 10.1186/s12876-021-01611-0. PMID: 33509102; PMCID: PMC7842074.

43 Shin YW, Bang BW, Kwon K, et al. Endoscopic application of new hemostatic powder in gastrointestinal bleeding. Endoscopy. 2018;50;OP006

44 Beyazit Y, Kurt M, Kekilli M, Goker H, Haznedaroglu IC. Evaluation of hemostatic effects of Ankaferd as an alternative medicine. Altern Med Rev. 2010 Dec;15(4):329-36. PMID: 21194248.

45 Haznedaroglu BZ, Haznedaroglu IC, Walker SL, Bilgili H, Goker H, Kosar A, Aktas A, Captug O, Kurt M, Ozdemir O, Kirazli S, Firat HC. Ultrastructural and morphological analyses of the in vitro and in vivo hemostatic effects of Ankaferd Blood Stopper. Clin Appl Thromb Hemost. 2010 Aug;16(4):446-53. doi: 10.1177/1076029609343706. Epub 2009 Oct 14. PMID: 19833624.

46 Gungor G, Goktepe MH, Biyik M, Polat I, Tuna T, Ataseven H, Demir A. Efficacy of ankaferd blood stopper application on non-variceal upper gastrointestinal bleeding. World J Gastrointest Endosc. 2012 Dec 16;4(12):556-60. doi: 10.4253/wjge.v4.i12.556. PMID: 23293725; PMCID: PMC3536852.

47 Ozaslan E, Purnak T, Yildiz A, Haznedaroglu IC. The effect of a new hemostatic agent for difficult cases of non-variceal gastrointestinal bleeding: Ankaferd blood stopper. Hepatogastroenterology. 2010 Mar-Apr;57(98):191-4. PMID: 20583410.

48 Yarali N, Oruc M, Bay A, Dalgic B, Bozkaya IO, Arıkoglu T, Kara A, Tunc B. A new hemostatic agent--Ankaferd blood stopper: management of gastrointestinal bleeding in an infant and other experiences in children. Pediatr Hematol Oncol. 2010 Nov;27(8):592-6. doi: 10.3109/08880018.2010.503337. Erratum in: Pediatr Hematol Oncol. 2014 Feb;31(1):107. Ankoglu, Tugba [corrected to Arıkoglu, Tugba]. PMID: 20863156.

49 Kurt M, Akdogan M, Onal IK, Kekilli M, Arhan M, Shorbagi A, Aksu S, Kurt OK, Haznedaroglu IC. Endoscopic topical application of Ankaferd Blood Stopper for neoplastic gastrointestinal bleeding: A retrospective analysis. Dig Liver Dis. 2010 Mar;42(3):196-9. doi: 10.1016/j.dld.2009.05.006. Epub 2009 Jun 21. PMID: 19540818.

50 Zulfikar OB, Emiroglu HH, Kebudi R. Nasogastric application of topical Ankaferd Blood Stopper for bleeding from primary esophageal adenocarcinoma in a child with disseminated intravascular coagulation. Dig Liver Dis. 2011 Mar;43(3):247-8. doi: 10.1016/j.dld.2010.10.002. Epub 2010 Dec 21. PMID: 21177146.

51 Tuncer I, Doganay L, Ozturk O. Instant control of fundal variceal bleeding with a folkloric medicinal plant extract: Ankaferd Blood Stopper. Gastrointest Endosc. 2010 Apr;71(4):873-5. doi: 10.1016/j.gie.2009.08.021. Epub 2009 Nov 17. PMID: 19922917.

52 Ozaslan E, Purnak T, Yildiz A, Haznedaroglu IC. Bleeding due to slippage of elastic band during variceal ligation: successful use of Ankaferd blood stopper. Indian J Gastroenterol. 2010 Jul;29(4):166-8. doi: 10.1007/s12664-010-0043-y. Epub 2010 Sep 3. PMID: 20814774.

53 Kurt M, Onal I, Akdogan M, Kekilli M, Arhan M, Sayilir A, Oztas E, Haznedaroglu I. Ankaferd Blood Stopper for controlling gastrointestinal bleeding due to distinct benign lesions refractory to conventional antihemorrhagic measures. Can J Gastroenterol. 2010 Jun;24(6):380-4. doi: 10.1155/2010/896819. PMID: 20559581; PMCID: PMC2898493.

54 Karaman A, Torun E, Gürsoy S, Yurci A, Ozbakir O. Efficacy of Ankaferd Blood Stopper in postpolypectomy bleeding. J Altern Complement Med. 2010 Oct;16(10):1027-8. doi: 10.1089/acm.2010.0089. PMID: 20954959.

Answers to this month's crossword puzzle:

1 B	A	2 R	R	3 E	T	4 T	S	■	■	5 H	O	6 T
I	■	E	■	R	■	I	■	7 O	■	O	■	E
8 L	A	C	T	O	S	E	■	9 S	O	L	A	R
E	■	T	■	D	■	■	■	T	■	I	■	M
■	10 W	A	11 V	E	■	12 B	I	O	13 P	S	Y	■
■	■	14 L	A	S	15 E	■	■	16 M	E	T	■	■
17 G	I	■	■	■	18 M	U	T	A	T	I	19 O	20 N
E	■	21 E	■	■	S	■	■	T	■	22 C	R	U
23 N	A	V	E	24 L	■	25 D	I	E	26 T	■	27 A	T
E	■	E	■	U	■	R	■	■	I	■	N	■
28 T	O	N	I	C	29 S	■	30 B	31 E	N	32 I	G	N
I	■	T	■	33 I	T	34 S	■	35 A	C	R	E	■
36 C	A	S	C	A	D	E	■	37 T	T	E	S	T