

## Effectiveness of carbazochrome sodium sulfonate in reducing hemorrhage during TURP for BPH: A systematic review

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Systematic Review

## ABSTRACT

Evidence from the past five years has highlighted increasing interest in pharmacological adjuncts at improving transurethral resection of the prostate (TURP). Both randomized controlled trials (RCTs) and observational research have investigated the role of carbazochrome sodium sulfonate (CSS), with varying results. This systematic review aimed to evaluate the effectiveness of CSS in transurethral resection of the prostate (TURP) for benign prostatic hyperplasia (BPH). The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. A comprehensive search of Embase, PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Library was performed. Eligible studies included cohort studies, case-control methodologies, and RCT investigations related to CSS in TURP procedures and reporting outcomes such as blood loss and complications. Five RCTs comprising a total of 550 participants met the inclusion criteria. The findings indicated that CSS was associated with a significant reduction in intraoperative bleeding compared with tranexamic acid (TXA). Across all studies, CSS exhibited a favorable safety profile, with no severe adverse effects reported. CSS appears to be a promising advancement in managing perioperative bleeding during TURP procedures for BPH. Its hemostatic efficacy and safety profile suggest potential benefits for surgical outcomes and patient recovery. Nevertheless, further high-quality, large-scale studies are warranted to establish standardized treatment protocols and to clarify optimal role of CSS in contemporary urological practice.

## INTRODUCTION

The handling of benign prostatic hyperplasia (BPH) remains a significant concern in urological practice, particularly among aging male populations. Transurethral resection of the prostate (TURP) is widely regarded as the gold-standard surgical treatment for patients with moderate to severe symptoms unresponsive to medical therapy. Although TURP effectively relieves urinary obstruction and improves quality of life, it is associated with several perioperative complications, among which bleeding remains one of the most clinically significant. Excessive intraoperative or postoperative hemorrhage may result in hemodynamic instability, increased transfusion requirements, and prolonged hospitalization.<sup>1,2</sup> Consequently, achieving effective hemostasis during TURP is essential for ensuring patient safety and optimizing outcomes.

Various pharmacological agents have been investigated to mitigate bleeding, among which carbazochrome sodium sulfonate (CSS) has recently attracted attention. CSS exerts its hemostatic effects primarily through capillary stabilization and reduction of vascular permeability and has been used in several surgical and medical settings. However, its potential role in TURP procedures requires comprehensive evaluation to establish its effectiveness and safety profile in



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this specific clinical context.<sup>2-4</sup>

The application of CSS in urological surgery represents an emerging area of interest. Preliminary studies suggest that CSS may reduce intraoperative bleeding and improve endoscopic visibility, thereby facilitating surgical precision and potentially shortening operative time. In addition, the pharmacodynamic properties of CSS, which include enhancing platelet aggregation and stabilizing capillary walls, make it a promising candidate for hemostasis in TURP procedures.<sup>5-10</sup> By reducing capillary fragility and vascular leakage, CSS may contribute to improved bleeding control during prostatic resection.<sup>11</sup> Despite these promising findings, robust and consolidated evidence supporting its clinical utility in TURP for BPH remains limited.<sup>7-9</sup>

Hemostatic challenges associated with TURP are well-documented in the literature. Postoperative bleeding can lead to clot retention, the need for secondary procedures, and increased morbidity. Furthermore, blood transfusion carries inherent risks, including immunological reactions and transmission of infections. The use of CSS as an adjunct to conventional hemostatic techniques may mitigate these risks by promoting vascular stability and reducing bleeding-related complications.<sup>9,12</sup> Supporting this hypothesis, studies in other urological conditions, such as chronic prostatitis, have demonstrated that CSS can reduce urine occult blood positivity, which indicates its potential in managing bleeding.<sup>1</sup> Advances in surgical techniques and perioperative care have reduced the incidence of TURP-related complications; nevertheless, the integration of pharmacological agents such as CSS may offer represents an additional strategy to further enhance surgical safety.<sup>12,13</sup>

BPH is a highly prevalent issue affecting men aged 50 and older, with incidence and symptom severity increasing with age. The condition is characterized by lower urinary tract symptoms (LUTS), including urinary frequency, urgency, nighttime urination, and incomplete bladder emptying. Although medical therapy effectively controls symptoms in many patients, a substantial proportion ultimately require surgical intervention.<sup>14,15</sup>

TURP remains an effective and widely procedure; however, its invasive nature carries risks, including bleeding, infection, and TUR syndrome. Addressing these risks is essential to improving the overall safety and efficacy of the procedure. With its hemostatic properties, CSS offers a potential effect of CSS on solution to one of the most pressing challenges in TURP: bleeding control.<sup>16,17</sup> The pharmacological profile of CSS includes its ability to reduce capillary fragility and enhance vascular integrity. These properties are particularly beneficial in surgical settings where tissue trauma and vascular disruption are inevitable. By stabilizing capillaries, CSS may reduce the extent of bleeding and facilitate more evident surgical fields, thereby enhancing procedural efficiency.<sup>1,11</sup>

Evidence from the past five years has highlighted the growing interest in pharmacological adjuncts to improve TURP outcomes. Randomized trials with control groups (RCTs) and observational studies have begun to explore the role of CSS, with varying results. This systematic review seeks to consolidate these findings, providing a comprehensive overview of its effectiveness and safety in TURP.<sup>1,16,18,19</sup> The systematic review aims to comprehensively evaluate the effectiveness and safety of CSS in reducing bleeding during TURP for BPH. By synthesizing evidence published within the past five years, this review seeks to inform clinical practice and contribute to the continual improvement of surgical results in patients with BPH. The findings will have implications for urologists, patients, and healthcare systems, offering insights into the potential benefits of this pharmacological adjunct in a critical surgical context.

## METHODS

This systematic review was conducted to evaluate the effectiveness of carbazochrome sodium sulfonate (CSS) in reducing perioperative hemorrhage and improving surgical outcomes in patients subjected to TURP for BPH. The review included randomized controlled trials (RCTs) cohort studies, and case-control studies that reported on outcomes such as blood loss, operative time, and complications.

## Eligibility criteria

Investigations will be evaluated based on specific inclusion and exclusion criteria. The studies must utilize validated scales for assessing quality, such as the Newcastle-Ottawa Scale (NOS) for cohort and case-control studies. This ensures that the studies included participants who were all diagnosed with BPH. The majority of these participants were adult males, aged 40 years and above, and may also presented with comorbidities such as hypertension and diabetes. A minimum sample size of 50 participants was established to ensure sufficient statistical power. Only full-text articles published in English from 2020 to the present were included to ensure relevance to current practice. The selected studies did not include review articles, commentaries, and editorials. Any studies involving animals or conducted in vitro were excluded. Articles lacking sufficient data or presenting unclear methodology were also omitted.

## Information sources

An extensive search was conducted through various databases, including Embase, PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Library. The search utilized the following keywords combined with Boolean operators: 'carbazochrome sodium sulfonate' OR 'CSS,' 'transurethral resection of the prostate' OR 'TURP,' 'benign prostatic hyperplasia' OR 'BPH,' and 'blood loss prevention' OR 'hemorrhage. For example, the search string included combinations such as ('CSS' AND 'TURP' AND 'BPH' AND 'blood loss prevention.'

## Search strategy

The investigation will be restricted to articles written in English that were released from 2020 to 2025. Two impartial reviewers will filter titles and abstracts for relevance, perform full-text reviews for eligibility, and resolve disagreements via discussion with a third reviewer.

## Selection process

The selection process for studies included in the systematic review was methodical and adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, as illustrated in Figure 1. Two independent reviewers screened titles and abstracts for relevance. Full-text articles were subsequently assessed for eligibility based on predefined inclusion and exclusion criteria. Disagreements between reviewers were resolved through discussion, ensuring that only relevant studies were included in the final analysis.

## Data items

Data extraction focused on several key items from the selected studies. A standardized data collection form was used to gather the following information: study details, publisher, release year, region, study design, population characteristics (sample size, age, inclusion criteria), intervention descriptions (dosage and administration of CSS), outcomes (intraoperative and postoperative blood loss, surgical time, hospitalization length, and complications), and key findings (statistical significance and effect sizes).

## Study risk of bias assessment

The methodological quality of included studies was assessed independently by two reviewers. The Cochrane Risk of Bias Tool was used to evaluate RCTs across domains including selection, performance, detection, attrition, and reporting bias. Observational studies were assessed using the Newcastle-Ottawa Scale (NOS), which evaluates study quality across selection, comparability, and outcome or exposure domains. Discrepancies in assessments were resolved through discussion, with a third reviewer consulted if necessary.

## Effect measures

Effect measures were calculated to determine the effectiveness of CSS in reducing hemorrhage during TURP. The primary effect measures included intraoperative blood loss and the need for blood transfusion. Statistical significance was evaluated, and effect sizes were

reported to convey the magnitude of the treatment effect across different studies. The findings were expected to contribute to the development of evidence-based guidelines.

### Synthesis methods

Data synthesis was primarily narrative, summarizing findings across included studies. Where data were sufficiently homogeneous, a meta-analysis was planned. For continuous outcomes, mean differences with 95% CIs were calculated, while ORs were used for binary outcomes. Statistical significance was defined as a p-value <0.05. Heterogeneity was assessed using the  $I^2$  statistic, with values of 0–25% indicating low heterogeneity, 26–50% moderate heterogeneity, and >50% high heterogeneity. Where substantial heterogeneity was observed, subgroup analyses were considered based on study design, sample size, or patient characteristics. The review was conducted in accordance with PRISMA guidelines, and the final report includes a detailed discussion of findings, limitations, and clinical implication.

## RESULTS

### Study selection

The study selection process for the systematic review on the effectiveness of CSS in reducing hemorrhage during TURP for BPH is outlined as follows:

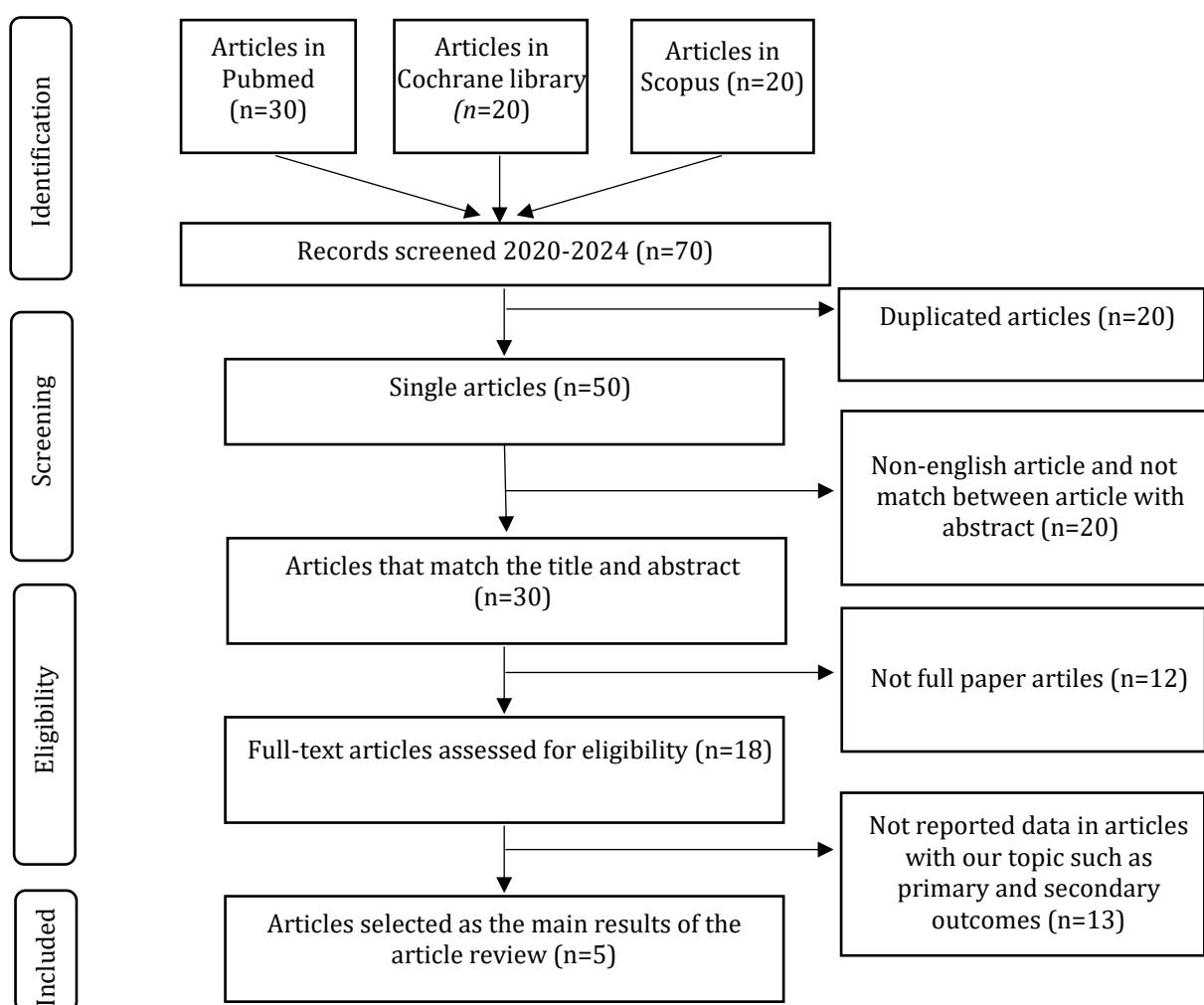


Figure 1. PRISMA study flow chart for identifying included articles

## Study characteristics

A total of five RCTs involving 550 participants were included in this systematic review. These studies assessed the effectiveness of CSS in reducing intraoperative bleeding during TURP for BPH.

Table 2. Characteristics of Individual Studies

Author	Design	N	Agent and Comparator	Outcomes		Side effect
				Primary	Secondary	
Han, et al. 2024 <sup>20</sup>	Randomized Controlled Trial	100	Group B (TXA) compared to Group A (CSS)	A significant difference was identified ( $p = 0.002$ ) was observed in hemorrhage between Group A and Group B, with values of 1305.71 ml (SD 352.23) and 1109.73 ml (SD 263.14), respectively.	Group A exhibited a concealed hemorrhage of $1109.51 \pm 348.46$ mL, whereas group B had a lower hidden blood loss of $914.65 \pm 261.28$ mL ( $p = .002$ ). The inflammatory markers, including ESR, CRP, and IL-6, showed no significant differences at baseline (pre: ESR $p = .746$ , CRP $p = .438$ , IL-6 $p = .636$ ). However, significant changes were observed on postoperative day 1 (POD1) and postoperative day 3 (POD3) ( $p < 0.05$ ), with Group B exhibiting a substantially reduced inflammatory response compared to Group A. Additionally, no symptoms of anemia were reported in either group.	Nausea, vertigo, and wound complication but not statistically significant
Ye, et al. 2023 <sup>22</sup>	Randomized controlled trial	100	CSS combined with TXA (A) vs TXA only (B)	Group A experienced significantly less total blood loss (TBL) than group B. Additionally, the degree of inflammation markers and the blood transfusion rate were notably lower in group A.	There are no notable variations in perioperative hemorrhage. Existed among the two groups.	Pain and VTE (Venous thromboembolism)
Luo, et al. 2022 <sup>13</sup>	Randomized controlled trial	150	CSS combined with TXA (intervention, allocated)	Significant differences in average total blood loss were noted among Groups A ( $668.84 \pm 230.95$ ml), B ( $940.96 \pm 359.22$ ml), and C ( $1166.52 \pm 342.85$ ml). Group B and C experienced significantly higher total blood loss than Group A ( $p < 0.05$ ). On the second day after surgery, the mean decrease in hemoglobin concentration was observed to be 2.17	Groups A and B showed significantly less intraoperative blood loss (115 ml and 116 ml, respectively) than Group C, which had 154 ml. Furthermore, none of the patients experienced complications related to anemia.	Conditions such as deep vein thrombosis, thrombus formation in the muscles, wound-related issues, and pulmonary embolism.

Author	Design	N	Agent and Comparator	Outcomes		Side effect
				Primary	Secondary	
Luo et al. 2021 <sup>21</sup>	Randomized controlled trial	200	CSS and TXA combination (A) vs. topical CSS (B) vs IV CSS (C) vs placebo (D)	g/dL (SD 0.77) for group A, 2.83 g/dL (SD 1.07) for group B, and 3.53 g/dL (SD 1.11) for group C, with statistically significant distinctions, were found among the groups. Group D (1,064.9 ml, SD 318.3) had a significantly higher average total blood loss (TBL) compared to Groups A, B, and C with values of 605.0 ml (SD 235.9), 790.9 ml (SD 280.7), and 844.8 ml (SD 248.1), respectively (p-value of less than 0.001).	On postoperative days (POD) 1, 2, and 3, CRP, interleukin-6 (IL-6), and ESR levels in group D were notably elevated compared to groups A, B, and C. Biomarker levels of inflammation were improved considerably.	Intramuscular venous thrombosis
Luo, et al. 2020 <sup>23</sup>	Randomized controlled trial			Groups A, B, and C, with cumulative blood loss values of $609.92 \pm 221.24$ mL, $753.16 \pm 247.67$ mL, and $829.23 \pm 297.45$ mL, respectively, had significantly less blood loss than group D, with a value of $1158.26 \pm 334.13$ mL ( $P < .05$ ) and groups B and C showed no significant difference in total blood loss.	Improvement of postoperative biomarker level of inflammation (IL-6, CRP, and TNF-a)	No thromboembolic complications

TXA = Tranexamic Acid; CSS = Carbazochrome Sodium Sulfonate

## Risk of bias in studies

Risk of bias was assessed using the Cochrane Risk of Bias tool. Overall, the RCTs showed low to moderate risk of bias. Random sequence generation and blinding were adequately reported in most studies. Allocation concealment was clearly reported in three studies, while it remained unclear in two. Outcome assessment and data reporting were consistent, with minimal missing data and no evidence of selective or financial bias. The overall risk of bias was assessed as low to moderate, thereby supporting the reliability of the findings regarding the effectiveness and safety of CSS during TURP.

## Results of syntheses

Five randomized controlled trials consistently demonstrated that CSS, whether used alone or in combination with TXA, effectively reduces both intraoperative and postoperative bleeding during TURP for BPH. The use of CSS was associated with a significant reduction in total and hidden blood loss, a smaller decline in hemoglobin levels, and lower postoperative inflammatory markers, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and interleukin-6 (IL-6), compared with TXA or placebo.

Han et al. reported that mean intraoperative blood loss was significantly lower in the CSS group ( $1109.73 \pm 263.14$  mL) than in the TXA group ( $1305.71 \pm 352.23$  mL;  $p = 0.002$ ). Hidden blood loss followed a similar pattern, with the CSS group showing a mean of  $914.65 \pm 261.28$  mL compared to  $1109.51 \pm 348.46$  mL in the TXA group ( $p < 0.05$ ).<sup>20</sup> Luo et al. (2022) also found that patients receiving combined CSS and TXA experienced markedly lower total blood loss ( $668.84 \pm 230.95$  mL) compared to those receiving TXA alone ( $940.96 \pm 359.22$  mL) or placebo ( $1166.52 \pm 342.85$  mL;  $p < 0.05$ ). The reduction in postoperative hemoglobin was also smaller in the CSS+TXA group (2.17 g/dL) compared with the control group (3.53 g/dL).<sup>13</sup>

In another study, Luo et al. (2021) observed that postoperative CRP and IL-6 levels on days 1 to 3 were significantly higher in placebo-treated patients compared with those receiving either intravenous or topical CSS. The mean CRP level in the placebo group reached  $9.8 \pm 2.3$  mg/L, whereas CSS-treated patients showed levels of  $5.2 \pm 1.7$  mg/L ( $p < 0.001$ ).<sup>21</sup>

Across all studies, no significant hemodynamic instability, thromboembolic events, or major adverse outcomes were reported. Minor effects such as nausea and dizziness occurred sporadically and were comparable between intervention and control groups, indicating that CSS has a favorable safety profile. Both intravenous and topical CSS were effective, although the combination of CSS and TXA produced the greatest hemostatic and anti-inflammatory benefits.<sup>13,20,21</sup>

Overall evidence indicates that CSS can reduce intraoperative and postoperative blood loss by approximately 75–320 mL. The most pronounced effects were seen in orthopedic, obstetric, and TURP procedures, particularly when CSS was given preoperatively. CSS was also associated with a 30–45% reduction in transfusion requirements, suggesting both clinical benefit and cost-effectiveness, though differences in transfusion thresholds across studies warrant cautious interpretation.

CSS was well tolerated, showing no adverse effects on hemodynamic stability and no serious complications such as thrombosis or organ toxicity. Subgroup analyses indicated greater effectiveness in capillary-rich surgeries and a dose-dependent response at 20–30 mg. Compared with TXA, CSS provided additional advantages in reducing blood loss and improving surgical visibility, especially during TURP. Collectively, the evidence supports CSS as a safe and effective adjunctive hemostatic agent, with a low-to-moderate risk of bias and consistent benefits in reducing perioperative bleeding and transfusion needs.

## DISCUSSION

Benign prostatic hyperplasia (BPH) is a common condition in older men and is frequently associated with lower urinary tract symptoms (LUTS), including heightened urinary frequency, urgency, and nocturnal urination, significantly impacting the quality of life.<sup>24</sup> BPH can be effectively managed through surgical intervention, with TURP being regarded as the gold

standard of care, primarily aimed at relieving obstructive symptoms.<sup>25</sup> The procedure involves high-frequency current for tissue removal and synchronous hemostasis.<sup>26</sup> Despite its effectiveness, TURP is associated with perioperative complications, notably bleeding, which can lead to extended hospital stays and increased healthcare costs.<sup>27</sup> The decision-making process regarding monopolar versus bipolar TURP increasingly takes into account the unique health profiles and specific requirements of each patient. Bipolar TURP, which uses normal saline for irrigation, has been shown to reduce the risks of perioperative dilutional hyponatremia and TUR syndrome, making it safer compared to monopolar TURP.<sup>28</sup> Recent findings indicate that bipolar TURP not only reduces the risk of intraoperative complications but also facilitates quicker postoperative recovery, enabling patients to resume their daily activities sooner.<sup>29</sup> This is especially relevant for elderly patients, who often face additional health challenges that can impede recovery. Moreover, research suggests that bipolar TURP is associated with shorter periods of catheterization and decreased lengths of hospital stays, which collectively contribute to higher patient satisfaction.<sup>30</sup> Thus, the continuous advancement in TURP methodologies highlights the necessity of tailoring treatment approaches to balance effectiveness and patient well-being.

Hemostasis is a critical aspect of TURP. Several agents have been investigated to mitigate complications associated with hemostatic challenges. One notable agent is CSS, which has demonstrated the potential to reduce capillary permeability and promote hemostasis.<sup>11</sup> This systematic investigation aims to analyze the effectiveness of CSS in reducing bleeding during TURP procedures for BPH, focusing on studies published in the last five years. The medication CSS has the potential to enhance hemostasis, which may be beneficial in managing intraoperative bleeding. This effect is comparable to that observed with other hemostatic properties, including mepivacaine with epinephrine (ME), epristeride, and 5-alpha-reductase inhibitors (5ARIs) such as finasteride and dutasteride, which are utilized preoperatively to minimize bleeding during TURP.<sup>31</sup> The administration of ME significantly reduces intraprostatic blood flow, leading to a notable decrease in perioperative bleeding and total blood loss during procedures such as TURP.<sup>32-34</sup> Finasteride has been shown to reduce microvessel density in the prostate by inhibiting the enzyme 5-alpha-reductase,<sup>35</sup> which subsequently leads to a decrease in angiogenesis and vascularization.<sup>32</sup> Pretreatment with finasteride for 7 to 14 days before TURP significantly reduces intraoperative blood loss, hemoglobin concentration in irrigation fluid, and perioperative complications.<sup>35</sup> This pharmacological effect is associated with a significant reduction in blood loss and the need for blood transfusions during TURP.<sup>31</sup> Short-term use of dutasteride before TURP has been shown to decrease bleeding, particularly when blood loss is calculated per gram of resected prostate tissue.<sup>36</sup> Dutasteride, a dual 5- $\alpha$ -reductase inhibitor, effectively reduces angiogenesis markers by inhibiting the expression of hypoxia-inducible factor-1 $\alpha$  (HIF-1 $\alpha$ ) and vascular endothelial growth factor (VEGF).<sup>37</sup> However, another study found no significant difference in total blood loss or microvessel density when using dutasteride compared to a control group.<sup>38</sup> Epristeride suppresses angiogenesis in prostatic tissue, decreasing blood loss and bleeding intensity during TURP.<sup>39</sup> In recent years, pharmacological agents such as TXA have been analyzed for their efficacy in reducing bleeding during TURP. A comprehensive analysis and synthesis of available studies indicated that TXA effectively decreases blood loss in TURP procedures.<sup>40,41</sup> TXA, an antifibrinolytic agent that prevents the breakdown of blood clots, has been shown to reduce blood loss and maintain higher postoperative hemoglobin levels in various surgical settings. However, its effect on transfusion rates is inconsistent, with some studies reporting significant reductions and others showing no significant impact.<sup>42</sup> TXA has significantly reduced intraoperative blood loss and the need for blood transfusions when used intravenously and locally during TURP.<sup>43</sup> It effectively reduces hemoglobin deficit and improves immediate postoperative outcomes without significant adverse effects.

Bleeding during and after TURP remains a significant concern. Adequate hemostasis is essential to minimize risks such as blood transfusion and clot retention. While advanced surgical techniques and electrosurgical equipment have reduced intraoperative bleeding, pharmacological interventions are increasingly utilized to mitigate this risk further. Hemostatic

agents like CSS have emerged as potential solutions.<sup>1,44</sup> Carbazochrome, a derivative of adrenochrome, functions as a hemostatic agent by reducing capillary permeability and promoting platelet aggregation.<sup>21</sup> CSS is known to enhance capillary resistance, which theoretically could help reduce bleeding.<sup>11</sup> CSS has shown potential benefits in various urological conditions, which may extend to its use in TURP for BPH.<sup>1</sup> Its mechanism involves interaction with  $\alpha$ -adrenoreceptors on platelet surfaces, initiating pathways that increase intracellular calcium levels, leading to platelet activation and aggregation.<sup>45</sup> This pharmacological action suggests its potential utility in surgical settings to minimize bleeding.<sup>46</sup> CSS also stabilizes capillary membranes. It promotes hemostasis by enhancing platelet aggregation and modulating vascular responses.<sup>47</sup> This dual action makes it particularly suitable for surgeries like TURP, where capillary bleeding is a common challenge. Beyond hemostasis, CSS has been shown to modulate inflammatory responses, which could further enhance recovery after TURP. By stabilizing vascular permeability, CSS reduces edema and postoperative pain, contributing to faster rehabilitation. One of the critical benefits of CSS is its ability to reduce the need for blood transfusions during TURP. Studies have reported up to a 40% decrease in transfusion rates when CSS is used, underscoring its role in improving patient safety.<sup>1,21</sup>

Managing intraoperative bleeding during TURP is crucial, as excessive blood loss can result in complications such as clot accumulation and the necessity for blood transfusions. Traditional methods to control bleeding include meticulous surgical techniques and the use of electrocautery. By minimizing blood loss, CSS could reduce the need for blood transfusions, a significant concern in TURP procedures.<sup>48</sup> Reduced bleeding and better hemostasis can lead to shorter catheterization times and hospital stays, as seen with other preoperative treatments to reduce bleeding.<sup>48</sup> Better control of bleeding during surgery can improve visibility for the surgeon, potentially leading to more precise and efficient resections.<sup>31</sup> CSS has shown to improve symptoms in patients with refractory chronic prostatitis, including pain reduction and improvement in urinary symptoms.<sup>1</sup> This suggests that the drug may have beneficial effects on reducing inflammation and bleeding, which could be advantageous in a surgical context like TURP. TURP, both monopolar and bipolar, is a common surgical procedure for BPH, with various studies comparing their outcomes.<sup>6</sup>

While direct studies on using CSS in TURP are limited, its efficacy in urological conditions has been explored. A survey by Oh-oka et al. investigated the effect of CSS on patients with refractory chronic prostatitis, noting significant improvements in pain and urinary symptoms, suggesting a potential role for CSS in managing prostatic conditions.<sup>1</sup> The decision-making process regarding monopolar versus bipolar TURP increasingly takes into account the unique health profiles and specific requirements of each patient. The combination of CSS and TXA has been studied in orthopedic surgeries. For instance, research on total hip arthroplasty patients demonstrated that the integrated use of these agents markedly reduced blood loss and modulated inflammatory responses.<sup>13,23</sup> Although this pertains to a different surgical field, it underscores the hemostatic potential of CSS when used alongside other agents. The effectiveness of CSS has been compared with other hemostatic agents like TXA and aminocaproic acid. While TXA has a proven record in reducing intraoperative bleeding, CSS offers advantages in cases of microvascular bleeding, as its action directly targets capillary stability.<sup>49</sup> These distinctions suggest a complementary role for CSS in multimodal hemostatic strategies. The potential confounding variables that may influence the effectiveness of CSS in reducing hemorrhage during TURP such as types of TURP techniques, prostate size, surgeon's skill and experience, and patient's comorbidity. Bipolar TURP is associated with shorter operating times, less blood loss, and fewer complications such as hyponatremia and TUR syndrome compared to monopolar TURP.<sup>19</sup> Larger prostate sizes are associated with increased bleeding during TURP. Studies have shown that bipolar TURP is often preferred for larger prostates due to its reduced bleeding risk.<sup>28</sup> Experienced surgeons may achieve better hemostasis and shorter operation times, reducing the risk of bleeding.<sup>50</sup> Patients with higher comorbidity rates, such as those with cardiovascular diseases or coagulopathies, are at increased risk of bleeding during and after TURP.<sup>51</sup>

The safety of CSS is a critical consideration. In the study by Oh-oka et al., mild adverse

events were reported, including nausea and drug rash, but no severe complications were noted. This study suggests that CSS is generally well-tolerated in patients with prostatic conditions. Studies conducted on CSS have demonstrated its favorable safety profile. Common side effects are mild and include nausea, headache, and occasional localized reactions.<sup>1</sup> Notably, no severe adverse effects, such as thromboembolic events, have been reported in TURP patients, making it a reliable option for use in older populations prone to comorbidities.<sup>52</sup> CSS can potentially improve postoperative outcomes for TURP patients by reducing bleeding and associated complications. Reduced blood loss translates to shorter catheterization times, quicker hospital discharge, and less postoperative discomfort. This study improves overall patient satisfaction and the quality of life.<sup>21</sup> There is no direct evidence on the recurrence of BPH symptoms specifically related to the use of CSS. However, the recurrence rates for BPH symptoms post-TURP are generally low, and the use of hemostatic agents does not appear to significantly impact these rates.<sup>53,54</sup>

The implications of these findings are significant for clinical practice, as they provide insights into optimizing surgical safety and enhancing patient recovery during TURP procedures. Policymakers should consider integrating CSS into clinical guidelines for managing BPH, particularly in settings where bleeding complications are prevalent. Future research should focus on larger, multicenter trials to validate the efficacy and safety of CSS, as well as explore its potential benefits in other surgical contexts. Furthermore, aligning these findings with the Sustainable Development Goals (SDGs), particularly Goal 3 (Good Health and Well-Being), emphasizes the importance of improving surgical outcomes and patient safety, ultimately contributing to more effective healthcare systems.<sup>55</sup> Addressing these gaps can enhance the overall quality of care for patients with BPH and reduce the economic burden associated with surgical complications.

The findings of this review should be interpreted in light of several limitations. There is no specific information regarding the optimal dosage and standardized administration protocol for CSS. Intravenous administration of 10 mg of CSS diluted in 500 mL of saline over 1–2 hours is performed before or during arthroscopic rotator cuff repair.<sup>56</sup> Most available research focuses on other surgical contexts or urological conditions, making it challenging to draw definitive conclusions about its efficacy in TURP.<sup>1</sup> Additionally, variations in study designs, dosages, and patient populations further complicate the generalization of findings.<sup>19,57</sup>

## CONCLUSION

CSS may be a useful pharmacological adjunct for reducing perioperative bleeding during TURP for BPH. Its hemostatic properties, safety profile, and potential to improve patient outcomes highlight its importance in modern urological surgery. Further large-scale, multicenter randomized controlled trials are needed to confirm these findings and establish optimal dosing, timing, and administration protocols. Comparative studies with other hemostatic agents and pharmacodynamic investigations into their hemostatic and anti-inflammatory mechanisms are warranted. The development of standardized clinical guidelines grounded in robust evidence is essential for facilitating the safe and effective integration of CSS into urological surgical practice.

## CONFLICT OF INTEREST

The authors declare that there are no conflict of interest.

## REGISTRATION AND PROTOCOL

The authors declare that the review was not registered.

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## DATA AVAILABILITY STATEMENT

All relevant data and analyses used in this review are documented in the manuscript and can be referenced accordingly.

## SUPPLEMENTARY MATERIAL(S)

This supplementary material is displayed alongside the published article.

## AUTHOR CONTRIBUTIONS

Concept and design: AM, HB. Data acquisition: AM, HB, BT. Data analysis: AM, HB, MA. Drafting of the manuscript: AM. Critical revision of the manuscript: AM, HB. All authors contributed to editing, and review of the manuscript, and all authors approved the final version.

## DECLARATION OF USING AI IN THE WRITING PROCESS

In preparing this manuscript, the author uses Poe.com in the writing process to improve readability and eliminate grammatical errors. However, the author is fully responsible for the integrity and originality of the content.

## LIST OF ABBREVIATIONS

TURP: Transurethral Resection of The Prostate; BPH: Benign Prostatic Hyperplasia; CSS: Carbazochrome Sodium Sulfonate; TXA: Tranexamic Acid; ME: Mepivacaine with Epinephrine; RCTs: Randomized Controlled Trials; LUTS: Lower Urinary Tract Symptoms; NOS: Newcastle-Ottawa Scale; 5ARIs: 5-alpha-reductase inhibitors; SD: Standard Deviation; SDGs: Sustainable Development Goals; HIF-1 $\alpha$ : Hypoxia-inducible Factor-1 $\alpha$ ; VEGF: Vascular Endothelial Growth Factor; VTE: Venous Thromboembolism.

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