

Comparative Study on the Effectiveness of Flavonoids in Postoperative Pain and Wet Anus after Hemorrhoidectomy: A Retrospective Cohort Study

Siripong Sirikurnpiboon*, Waranthorn Somjinda

Division of Colorectal Surgery, Department of General Surgery, Rajavithi Hospital, College of Medicine, Rangsit University, Bangkok 10400, Thailand

***Corresponding author:**

Siripong Sirikurnpiboon, MD
Division of Colorectal Surgery
Department of General Surgery
Rajavithi Hospital
College of Medicine, Rangsit University
2 Paholyothin road, Rachatewi
Bangkok 10400, Thailand
Tel: + [66] [2-206-2900]
E-mail: laizan99@hotmail.com

ABSTRACT

Background: Hemorrhoidectomy is the conventional intervention for symptomatic or high-grade hemorrhoids; yet, problems such as postoperative discomfort, wound dehiscence, and moisture in the anal region are prevalent. Moist anal regions considerably affect patient comfort and hygiene yet remain inadequately researched. **Objectives:** To assess the efficacy of flavonoids in alleviating postoperative pain and the occurrence of wet anus.

Materials and Methods: A retrospective cohort analysis was performed with 180 individuals who underwent hemorrhoidectomy from 2017 to 2022. Patients were categorized into a flavonoid group (n = 91) and a control group (n = 89). Postoperative outcomes, including pain levels (at 6 hours and the following morning), and the incidence of moist anus, pruritus ani, and wound complications at 14 days postoperatively (POD 14), were evaluated alongside acetaminophen usage.

Results: The occurrence of wet anus at postoperative day 14 was markedly reduced in the flavonoid group (18.7% vs. 67.4%, $p < 0.001$), as was pruritus ani (18.7% vs. 56.2%, $p < 0.001$). Pain scores at 6 hours postoperatively were comparable (7.22 vs. 7.25, $p = 0.891$), however the subsequent morning scores were significantly reduced in the flavonoid group (6.11 vs. 6.73, $p = 0.017$). The intake of acetaminophen was markedly reduced in the flavonoid group (1069.6 mg compared to 1631.6 mg, $p < 0.001$). Wound dehiscence occurred less frequently (16.5% compared to 25.8%, $p = 0.045$; OR = 0.473, 95% CI: 0.226–0.993).

Conclusions: Flavonoids markedly diminished the occurrence of moist anal conditions and anal pruritus, and may decrease the necessity for analgesics and wound-related problems. These data indicate the supplementary application of flavonoids in postoperative management after hemorrhoidectomy.

Keywords: flavonoid, hemorrhoidectomy, wet anus, postoperative pain, pruritus ani

INTRODUCTION

Hemorrhoidal disease, affecting up to 75% of the general population during their lifetime, is one of the most prevalent anorectal conditions encountered in surgical practice (1). While conservative management with dietary modification and phlebotonic agents suffices for early-stage disease, excisional hemorrhoidectomy remains the definitive treatment for symptomatic grade III–IV

Received: 29.04.2026

Accepted: 16.06.2026

Copyright © Celsius Publishing House
www.sgo-iasgo.com

hemorrhoids (2). Despite its efficacy, the procedure carries significant postoperative morbidity—including pain lasting 2–3 weeks, hemorrhage, wound infection, and perianal discharge (clinically termed “wet anus”)—which substantially impairs recovery (2).

Micronized purified flavonoid fraction (MPFF) exerts pleiotropic pharmacodynamic effects directly relevant to the post-hemorrhoidectomy milieu: it enhances venous tone, reduces capillary hyperpermeability, promotes lymphatic drainage, inhibits leukocyte-endothelium adhesion, and attenuates reactive oxygen species in inflamed peri-operative tissue (3). Multiple randomized controlled trials (RCTs) and meta-analyses have confirmed that MPFF significantly reduces postoperative pain and bleeding (4-6). However, its efficacy in mitigating wet anus - a clinically significant and underresearched complication driven by surgical inflammation and lymphatic congestion - has not been systematically investigated.

This study aimed to evaluate the efficacy of adjunctive oral flavonoids in reducing postoperative wet anus, pain, pruritus ani, and analgesic consumption following closed hemorrhoidectomy, comparing outcomes between patients who received flavonoids and those who did not.

MATERIALS AND METHODS

Research Design

The researchers filed the study protocol, which received approval from the Institutional Review Board at Rajavithi Hospital. This research was structured as a retrospective cohort study. The research group comprised patients diagnosed with hemorrhoids who received hemorrhoidectomy at Rajavithi Hospital from January 1, 2017, to December 31, 2022.

Individuals Involved - Inclusion Criteria

All patients participating in this study exhibited symptomatic grade III internal hemorrhoids as per the Goligher classification, validated via clinical examination and anoscopy prior to surgical surgery. Patients with grade I, II, or IV hemorrhoids were omitted from the analysis to maintain uniformity in surgical difficulty. All patients had hemorrhoidectomy at Rajavithi Hospital during the research period. - Patients possessing comprehensive medical data pertaining to surgical outcomes, including pain ratings, hemorrhage, and complications. - Patients having unequivocal documentation of either getting or not receiving flavonoids.

Exclusion Criteria

Patients had inadequate medical records or lacking critical data necessary for analysis. Individuals having a history of allergies or significant adverse reactions associated with flavonoid use.

Ethical Approval

The study protocol was approved by the Institutional Review Board of Rajavithi Hospital (IRB No. 104/2568). Given the retrospective nature of this study and the use of de-identified existing medical records, the IRB granted a waiver of individual informed consent in accordance with applicable institutional guidelines for minimal-risk retrospective research. Patient confidentiality was maintained throughout the study.

Randomization and Blinding

The administration of flavonoids was not randomized but was entirely dependent on individual surgeon preference and their routine postoperative care protocols, rather than the severity of the disease or specific patient characteristics. This routine-based prescribing pattern helps mitigate potential confounding by indication.

Interventions

Patients were categorized into two groups according to their postoperative therapy.

1. *Flavonoid Group*: Patients administered oral flavonoids at a dose of 3,000 mg/day from days 1 to 3 and 2,000 mg/day from days 4 to 7 postoperatively.
2. *Control Group*: Patients who did not get flavonoids following surgery.

Operative Interventions

All patients received a closed hemorrhoidectomy of a solitary hemorrhoidal column with the Ferguson method. Cases requiring the excision of several hemorrhoidal columns were removed to mitigate heterogeneity in wound load that might independently affect postoperative discharge and discomfort. The surgeries were conducted by colorectal surgeons.

Standardized Postoperative Procedure

All patients in both cohorts were administered a consistent standardized postoperative medication

protocol comprising: Metronidazole (500 mg orally thrice daily for 7 days), Psyllium husk (1 sachet daily for 14 days), NSAIDs (diclofenac, 50 mg orally thrice daily for 5 days), Paracetamol (500–1,000 mg orally every 6 hours as required, with total daily intake documented)

The sole distinction in postoperative care between the two groups was the inclusion of oral flavonoids, delivered at the operating surgeon's discretion. Surgeons who consistently included flavonoids in their multimodal recovery protocols prescribed them to all patients, but those adhering to conventional treatment without phlebotonics did not. This prescription trend remained stable throughout the research period and was the foundation for group allocation in this retrospective cohort.

Performance Metrics

Principal outcomes - postoperative pain

Evaluated utilizing the Visual Analog Scale (VAS, 0–10) at 6 hours and the following morning post-surgery. The scores were obtained retrospectively from standard nursing records.

Wet anus

Characterized by continuous serosanguinous or serous exudate from the surgical site. An assessment was conducted on POD 14 via clinical history gathering (concerning ongoing wetness or dressing alterations) and physical examination (to detect obvious discharge or stains on dressings). The classification of wet anus employed a two-tiered methodology: 1) a binary result (present/absent) and 2) a severity score derived from the discharge/moisture subscale of the validated Proctological Symptom Scale (PSS)(7), utilizing a visual analog scale ranging from 0 (no discharge) to 10 (severe persistent discharge). A PSS discharge score of ≥ 3 was established as the criterion to diagnose clinically significant moist anus, in accordance with existing normative data.

Secondary outcomes

The occurrence of pruritus ani, postoperative hemorrhage, wound dehiscence, anal mucosa ectropion, and fecal incontinence (evaluated using the Wexner score) on postoperative day 14. - Aggregate acetaminophen intake.

Statistical Analysis

To address baseline disparities between groups observed after data assessment, a 1:1 propensity

score matching (PSM) was conducted before outcome analysis. Propensity scores were calculated via a multivariate logistic regression model that included all clinically pertinent baseline covariates: age, sex, BMI, ASA classification, presence of comorbidities, and symptom duration. Matching was conducted utilizing a nearest-neighbor approach with a caliper width of 0.2 standard deviations of the logit of the propensity score, without replacement. The equilibrium between the matched groups was evaluated by analyzing standardized mean differences (SMD), with an SMD < 0.10 being suggestive of sufficient balance.

Subsequent to matching, descriptive statistics included categorical data as frequencies and percentages, and continuous variables were presented as mean $\pm$ standard deviation (SD) or median and interquartile range (IQR). In univariate analysis, categorical variables were compared utilizing the Chi-square test or Fisher's exact test, while continuous variables were assessed using the Student's t-test or Mann-Whitney U test. Subsequently, multivariable binary logistic regression was conducted to verify independent relationships. Results were presented as adjusted odds ratios (aOR) accompanied by 95% confidence intervals (CI). A p-value less than 0.05 was deemed statistically significant.

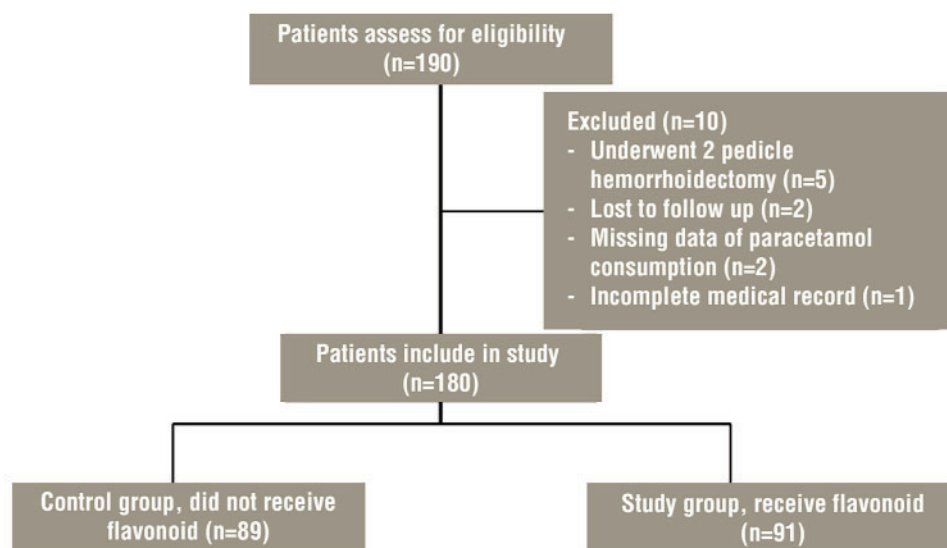
RESULT

A total of 190 patients were initially evaluated for eligibility (*fig. 1*). Ten patients were removed for the following reasons: five underwent only 2-pedicle hemorrhoidectomy, two were lost to follow-up, two had missing data on paracetamol usage, and one had incomplete medical records. As a result, the final analysis comprised 180 patients, with 91 assigned to the flavonoid group and 89 to the control group. The baseline parameters, such as age, sex, BMI, and ASA status, were mostly analogous across the two groups. As shown in *table 1*. The flavonoid group had a greater percentage of patients without comorbidities (86.8% vs. 64.0%, $p=0.036$) and a prolonged duration of symptoms (33.0% vs. 16.9%, $p=0.028$).

Postoperative Pain

No significant difference was found at 6 hours post-surgery (7.22 vs. 7.25, $p=0.891$). However, the flavonoid group reported significantly lower pain scores the next morning (6.11 vs 6.73, $p=0.017$). As shown in *table 2*.

Figure 1 - Flowchart of the study population selection process according to the STROBE statement



Wet Anus at POD 14

The incidence was markedly lower in the flavonoid group (18.7%) compared to the control group (67.4%) with $p < 0.001$ (OR 0.084; 95% CI: 0.041–0.173). To confirm the independent effect of flavonoids on reducing wet anus, a multivariable logistic regression was performed, as shown in *table 3*. After adjusting for potential confounders including comorbidities and

symptom duration, flavonoid use remained a significant independent protective factor against wet anus at POD 14 (Adjusted OR 0.075; 95% CI: 0.034–0.165; $p < 0.001$), as shown in *table 4*. Similarly, multivariable analysis was conducted for high postoperative pain scores in the next morning, defined as a Visual Analog Scale (VAS) score > 6 . Flavonoid use was identified as the only independent factor significantly associated with a reduction in these high pain scores (Adjusted OR

Table 1 - Demographic data

	Flavonoid (n=91)(%)	Non-flavonoid (n=89) (%)	p-value
Age			
< 60 years	84 (92.3)	75 (84.3)	0.093
Sex			
Female	51 (56.0)	48 (53.9)	0.776
BMI			
≥ 25 kg/m ²	25 (27.5)	24 (27.0)	0.939
ASA classification			
Class I	77 (84.6)	63 (70.8)	0.051
Class II	13 (15.4)	26 (29.2)	
Co-morbidities			
Non	79 (86.8%)	57 (64.0%)	0.036
Duration of symptom			
> 3 months	30 (33.0%)	15 (16.9%)	0.028
Anesthetic method			
Spinal anesthesia	41 (45.1%)	34 (38.2%)	0.351
Local anesthesia	50 (54.9%)	55 (61.8%)	0.351

Table 2 - Primary outcome

	Flavonoid (n=91)(%)	Non-flavonoid (n=89) (%)	p-value
Wet anus at POD#14 (%)	17 (18.7%)	60 (67.4%)	<0.001
Pain score at 6 hrs (mean±S.D.)	7.22 ± 2.03	7.25 ± 1.77	0.891
Pain score next morning (mean±S.D.)	6.11 ± 2.05	6.73 ± 1.20	0.017
Mean paracetamol dose (mg) (mean±S.D.)	1,069.6±795.55	1,631.6±997.89	< 0.001

Table 3 - Multivariable logistic regression analysis of factors associated with wet anus at POD 14

Variable	Crude OR (95% CI)	p-value	Adjusted OR (aOR) (95% CI)	p-value
Flavonoid use (Yes vs. No)	0.084 (0.041–0.173)	<0.001	0.075 (0.034–0.165)	<0.001*
Comorbidity (None vs. Has)	1.423 (0.781–2.593)	0.036	1.120 (0.450–2.785)	0.806
Symptom duration (< 3 vs. ≥ 3 months)	0.455 (0.223–0.926)	0.028	1.342 (0.582–3.094)	0.490

Table 4 - Multivariable logistic regression analysis for high pain score in the next morning

Variable	Crude OR (95% CI)	p-value	Adjusted OR (aOR) (95% CI)	p-value
Flavonoid Use (Yes vs. No)	0.112 (0.058–0.215)	<0.001	0.082 (0.040–0.168)	<0.001*
Comorbidity (None vs. Has)	1.350 (0.720–2.530)	0.036	1.050 (0.420–2.610)	0.916
Symptom Duration (< 3 vs. ≥ 3 months)	0.520 (0.280–0.960)	0.028	1.210 (0.540–2.720)	0.645

0.082; 95% CI: 0.040–0.168; $p < 0.001$), independent of baseline clinical imbalances such as comorbidities and symptom duration.

Anal Pruritus

Substantially reduced in the flavonoid group (18.7% compared to 56.2%, $p < 0.001$). Wound dehiscence occurred much less often in the flavonoid group (16.5% vs to 25.8%, $p = 0.045$). The average acetaminophen dosage was markedly reduced in the flavonoid group (1,069.6 mg compared to 1,631.6 mg, $p < 0.001$).

No instances of anal mucosa ectropion were seen in either group at postoperative day 14 (0% vs. 0%, $p = \text{N/A}$). This result aligns with the utilized single-column closed method and the meticulous maintenance of anoderm throughout the operation. Postoperative complication showed in *table 5*.

This retrospective study found no recorded significant side effects or allergic responses associated with flavonoid consumption in the medical records of the flavonoid group. Additional problems, including postoperative hemorrhage and fecal incontinence, exhibited no statistically significant variations between the two research cohorts.

DISCUSSION

This retrospective cohort study of 180 patients

demonstrated that adjunctive oral MPFF (3,000 mg/day for days 1–3, then 2,000 mg/day for days 4–7) following single-column closed hemorrhoidectomy significantly reduced wet anus at POD 14 (18.7% vs. 67.4%; $p < 0.001$), pruritus ani (18.7% vs. 56.2%; $p < 0.001$), next-morning pain (VAS 6.11 vs. 6.73; $p = 0.017$), total acetaminophen consumption (1,069.6 vs. 1,631.6 mg; $p < 0.001$), and wound dehiscence (16.5% vs. 25.8%; $p = 0.045$). Multivariable logistic regression confirmed that flavonoid use was the sole independent predictor of both reduced wet anus (aOR 0.075; 95% CI: 0.034–0.165) and lower high postoperative pain the following morning (aOR 0.082; 95% CI: 0.040–0.168), independent of baseline differences in comorbidities and symptom duration.

MPFF's pleiotropic pharmacodynamic profile underpins these findings: by suppressing adhesion molecule expression (ICAM-1, VCAM-1, E-selectin) on venular endothelium, it reduces the leukocyte-mediated inflammatory cascade; by alleviating microvascular hyperpermeability and augmenting lymphatic contractility, it limits the production and facilitates the clearance of perianal exudate; and its antioxidant properties attenuate reactive oxygen species in inflamed peri-operative tissues (3,8). These interconnected mechanisms directly explain the reductions in wet anus, pruritus ani, pain, and wound dehiscence observed across the cohort.

The most striking finding was the substantial

Table 5 - Postoperative complication

	Flavonoid (N=91)(%)	Non-flavonoid (N=89)(%)	p-value
Pruritus ani (%)	17 (18.7)	50 (56.2)	< 0.001
Wound dehiscence (%)	15 (16.5)	22 (25.8)	0.045
Postoperative bleeding	3 (3.3)	8 (9.0)	0.111
Gas incontinence (%)	2 (2.2)	0 (0)	0.160
Wexner's score (mean±S.D.)	0.06±0.5	0.18±0.7	0.207
Anal mucosa ectropion (%)	0 (0)	(0)	N/A

reduction in wet anus at POD 14 (OR 0.084; aOR 0.075; $p < 0.001$) an outcome seldom designated as a primary endpoint in prior flavonoid research. Wet anus arises primarily from surgical inflammation elevating capillary permeability, generating serous and serosanguinous exudate, compounded by impaired lymphatic clearance of perianal edema. MPFF targets both pathways directly (3, 8). Cospite's pivotal double-blind RCT demonstrated that MPFF markedly reduced anal discharge in acute hemorrhoidal disease (9), and the systematic review by Sheikh et al. (6) confirmed a significant effect through pooled analyses. Most directly comparable, Lee et al. (4) employed a nearly identical dosing regimen (3,000 mg/day $\times$ 4 days then 2,000 mg/day $\times$ 3 days) and reported a striking reduction in purulent discharge at 18 days post-closed hemorrhoidectomy (14.8% vs. 63.0%; $p < 0.005$). The aOR of 0.075, maintained after controlling for comorbidities and symptom duration, confirms that this effect is pharmacologically mediated rather than a product of patient selection.

The reduction in pruritus ani (18.7% vs. 56.2%; $p < 0.001$) is mechanistically inseparable from the reduction in wet anus. Perianal moisture and serous leakage are the primary triggers of the itch-scratch cycle, which, once established, becomes self-perpetuating (10). A narrative review by Jakubauskas and Dulskas (11) confirmed that increased perianal moisture and fecal contamination remain the dominant initiating factors for this cycle, whether from physiological or surgical sources. By reducing the volume of perianal surgical exudate, MPFF disrupts this mechanism at its inception—consistent with La Torre et al.'s observation of reduced pruritus intensity at POD 3 post-Milligan-Morgan hemorrhoidectomy (12) and with the favorable trend noted in the systematic review by Sheikh et al. (6). Our findings extend these observations to POD 14, demonstrating a clinically meaningful absolute risk reduction of 37.5 percentage points, suggesting that sustained perianal dryness translates into durable symptom relief beyond the immediate postoperative period.

About the postoperative pain. The absence of a between-group difference in 6-hour VAS scores (7.22 vs. 7.25; $p = 0.891$) is consistent with MPFF's pharmacokinetic profile, as its venoactive and anti-inflammatory activities require several hours to attain clinical significance (3,13). By the following morning, MPFF use was associated with significantly lower pain scores and was the sole independent predictor of non-high pain on multivariate analysis (aOR 0.082; $p < 0.001$), consistent with Colak et al.'s demonstration of reduced VAS scores on days 2, 3, and 7 and diminished intramuscular

analgesic demand (14). The meta-analysis by Fu et al. (8), encompassing 22 RCTs and 2,335 patients, confirmed that the 1,800–2,700 mg/day dose range corresponding to our protocol was particularly efficacious for pain and edema reduction. The meta-analysis by Pitesa et al. (15) independently demonstrated a pooled standardized mean difference in pain of -0.66 (95% CI: -0.82 to -0.52 ; $p < 0.00001$) across 10 RCTs. The concomitant reduction in acetaminophen consumption (1,069.6 vs. 1,631.6 mg; $p < 0.001$) reinforces findings from Rabelo et al.'s recent double-blind RCT (16) and from Filingeri et al. (17), who documented reduced tenesmus at days 7, 15, and 30 post-hemorrhoidectomy. In a multimodal analgesia framework, minimizing non-opioid analgesic burden reduces the risk of drug-related adverse events and may shorten convalescence in outpatient settings.

Wound dehiscence was significantly less frequent in the flavonoid group (16.5% vs. 25.8%; $p = 0.045$; OR 0.473; 95% CI: 0.226–0.993). MPFF's anti-edematous action reduces tissue tension at wound margins, preserving primary closure integrity. Flavonoids particularly hesperidin promote wound healing through angiogenesis, collagen deposition, and suppression of inflammatory cell infiltration via TGF- β , NF- κ B, and MAPK/ERK signaling pathways (18). A recent experimental study by Kusumo et al. (19) demonstrated that diosmin-hesperidin reduces inflammatory tissue edema, modulates MMP-9 activity, and augments TGF- β expression in hemorrhoid models, providing mechanistic support for MPFF's structural wound-healing benefits beyond symptom relief. Enhanced microvascular perfusion of wound edges may additionally reduce the anaerobic micro-environment that predisposes to bacterial colonization and dehiscence (20).

Postoperative bleeding was numerically lower in the flavonoid group (3.3% vs. 9.0%) but did not reach significance ($p = 0.111$), likely due to the low absolute event rate in both cohorts. This is consistent with Ba-bai-ke-re et al. (21), who observed a non-significant trend toward reduced bleeding with flavonoids. Meta-analytic data, however, firmly support an anti-hemorrhagic effect: Sheikh et al. (6) reported an OR of 0.082 (95% CI: 0.027–0.250; $p < 0.001$), and Pitesa et al. (13) an OR of 0.13 ($p < 0.00001$). The study was likely underpowered to detect this effect at the observed event rates. Beyond symptomatic endpoints, the open-label RCT by Shelygin et al. (22) demonstrated that postoperative MPFF significantly reduces thrombosis and edema of mucocutaneous bridges, improves patient-reported outcomes, and prevents peri-

anal skin tag formation at 60 days, confirming that MPFF's benefits extend to structural wound-healing outcomes with potential long-term relevance.

Limitation

Several limitations of this investigation require consideration. The retrospective, non-randomized, single-center approach inherently increases selection bias, since the prescription of flavonoids was determined by individual surgeon judgment rather than through randomization. Despite multivariable logistic regression mitigating the influence of observed confounders, residual confounding from unmeasured variables—such as dietary fiber consumption, analgesic choice, or nursing directives—remains a possibility. The evaluation of wet anus and pruritus ani was based on clinical history and physical examination during a solitary postoperative visit (day 14), instead of utilizing validated patient-reported outcome measures (e.g., the Hemorrhoidal Disease Symptom Score), potentially introducing subjectivity in outcome categorization. The brief follow-up duration fails to encompass long-term outcomes, including recurrence, quality of life, or patient satisfaction. Fourth, despite the enforcement of technical consistency through closed hemorrhoidectomy, the involvement of numerous surgeons with differing levels of expertise may have introduced inter-operator heterogeneity in tissue handling, potentially affecting healing results. Future prospective, double-blind randomized controlled trials utilizing standardized outcome measures and prolonged follow-up are necessary to corroborate these findings and to establish appropriate dosage protocols for various grades of hemorrhoidal illness.

CONCLUSIONS

This study presents compelling evidence that the supplementary administration of oral flavonoids markedly decreases the occurrence of anal moisture, anal itching, and postoperative discomfort after hemorrhoidectomy. These findings advocate for the regular use of flavonoids in postoperative care procedures to improve patient recovery and satisfaction.

Conflicts of Interest

The authors declare no conflict of interests.

Ethics of Approval

The study was approved by Rajavithi ethical broad committee.

REFERENCES

- Nelson RL, Abcarian H, Davis FG, Persky V. Prevalence of benign anorectal disease in a randomly selected population. *Dis Colon Rectum*. 1995;38(4):341-4.
- Sayfan J. Complications of Milligan-Morgan hemorrhoidectomy. *Dig Surg*. 2001;18(2):131-3.
- Lyseng-Williamson KA, Perry CM. Micronised purified flavonoid fraction: A review of its use in chronic venous insufficiency, venous ulcers and haemorrhoids. *Drugs*. 2003;63(1):71-100.
- Lee HW, Lee WY, Chun HK. Clinical effects of Venitol on complications after hemorrhoidectomy: prospective randomized and placebo-controlled trial. *J Korean Soc Coloproctol*. 1998;14:761-6.
- Perera N, Liolitsa D, Iype S, Croxford A, Yassin M, Lang P, et al. Phlebotonics for haemorrhoids. *Cochrane Database Syst Rev*. 2012; 8:CD004322.
- Sheikh P, Lohsiriwat V, Shelygin Y. Micronized Purified Flavonoid Fraction in Hemorrhoid Disease: A Systematic Review and Meta-Analysis. *Adv Ther*. 2020;37(6):2792-812.
- Kraemer M, Kara D, Rzepisko M, Sayfan J. A simple tool to evaluate common disorders: validation of a "proctological symptom scale". *Int J Colorectal Dis*. 2015;30(5):679-82.
- Fu H, Guo W, Zhou B, Liu Y, Gao Y, Li M. Efficacy and safety of micronized purified flavonoid fractions for the treatment of post-operative hemorrhoid complications: A systematic review and meta-analysis. *Phytomedicine*. 2022;104:154244.
- Cospite M. Double-blind, placebo-controlled evaluation of clinical activity and safety of Daflon 500 mg in the treatment of acute hemorrhoids. *Angiology*. 1994;45(6 Pt 2):566-73.
- Ansari P. Pruritus Ani. *Clin Colon Rectal Surg*. 2016;29(1):38-42.
- Jakubauskas M, Dulskas A. Evaluation, management and future perspectives of anal pruritus: a narrative review. *Eur J Med Res*. 2023;28(1):57.
- La Torre F, Nicolai AP. Clinical use of micronized purified flavonoid fraction for treatment of symptoms after hemorrhoidectomy: results of a randomized, controlled, clinical trial. *Dis Colon Rectum*. 2004;47(5):704-10.
- Sirikurnpiboon S, Jivapaisarnpong P. Botulinum Toxin Injection for Analgesic Effect after Hemorrhoidectomy: A Randomized Control Trial. *J Anus Rectum Colon*. 2020;29;4(4):186-192.
- Colak T, Akca T, Dirlik M, Kanik A, Dag A, Aydin S. Micronized Flavonoids in Pain Control After Hemorrhoidectomy: A Prospective Randomized Controlled Study. *Surg Today*. 2003;33(11):828-32.
- Pitesa R, Yuen WYR, Hill AG. Flavonoids and post haemorrhoidectomy recovery: a systematic review and meta-analysis. *ANZ J Surg*. 2024;94(9):1480-1490.
- Rabelo FEF, Lacerda-Filho A, Mansur ES, de Oliveira FH, de Queiroz FL, França-Neto PR, et al. Benefits of flavonoid and metronidazole use after excisional hemorrhoidectomy: a randomized double-blind clinical trial. *Tech Coloproctol*. 2021;25(8):949-55.
- Filingeri V, Buonomo O, Sforza D. Use of flavonoids for the treatment of symptoms after hemorrhoidectomy with radiofrequency scalpel. *Eur Rev Med Pharmacol Sci*. 2014;18(5):612-6.
- Zulkefli N, Che Zahari CNM, Sayuti NH, Kamarudin AA, Saad N, Hamezah HS, Bunawan H, Baharum SN, Mediani A, Ahmed QU, Ismail AFH, Sarian MN. Flavonoids as Potential Wound-Healing Molecules: Emphasis on Pathways Perspective. *Int J Mol Sci*. 2023; 27;24(5):4607.
- Hidayat Budi Kusumo M, Prayitno A, Soetrismo, Laqif A. Synergistic therapeutic approach for hemorrhoids: integrating mesenchymal stem cells with diosmin-hesperidin to target tissue edema and inflammation. *Arch Med Sci*. 2024;20(5):1556-1566.
- Medkova YS, Tulina I, Yudina V, Abdullaev R, Shcherbakova V, Novikov I, Nikonov A, Tsarkov P. Efficacy of Micronized Purified Flavonoid Fraction in the Posthemorrhoidectomy Period Trial: Open-Label Randomized Controlled Trial. *Dis Colon Rectum*. 2024;67(6): 826-833.
- Ba-bai-ke-re MM, Huang HG, Re WN, Fan K, Chu H, Ai EH, et al. How we can improve patients' comfort after Milligan-Morgan open haemorrhoidectomy. *World J Gastroenterol*. 2011;21;17(11):1448-56.
- Sergeevna Medkova Y, Tulina I, Yudina V, Abdullaev R, Shcherbakova V, Novikov I, et al. Efficacy of Micronized Purified Flavonoid Fraction in the Posthemorrhoidectomy Period Trial: Open-Label Randomized Controlled Trial. *Dis Colon Rectum*. 2024;67(6): 826-833.