Management of Hemorrhoids – A Look into the Role of Diosmin

Reviewed by:

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Introduction

Hemorrhoids are a common anorectal condition characterized by the symptomatic enlargement and distal displacement of normal anal cushions.[1] Historical evidence of hemorrhoids dates back to 1700 BC, with Egyptian papyrus documenting treatments.[2] Multiple factors, such as constipation and prolonged straining, contribute to hemorrhoid development.[1] Hemorrhoids can occur at any age and affect both men and women.[3] Affecting millions globally, they pose a significant medical and socioeconomic challenge.[1]

Burden of hemorrhoids

- **Leading diagnosis:** 4th leading outpatient gastrointestinal diagnosis[4]
- **Prevalence:** 4.4% in the general population; up to 36.4% in general practice[3]
- **Lifetime risk:** 75% of the population will suffer from hemorrhoids at some time during their lives[5]
- **Age-specific prevalence:** At least 50% of individuals over 50 have experienced symptoms.[3]

Pathophysiology of hemorrhoids

The pathophysiology of hemorrhoid development is complex and not completely elucidated. The outdated varicose vein theory, which linked hemorrhoids to varicose veins, has been replaced as hemorrhoids and anorectal varices are distinct conditions.[1] Several theories have been proposed, such as sliding anal canal lining, hyperperfusion of the hemorrhoid plexus, vascular abnormalities, tissue inflammation, and internal rectal prolapse.[6]

The most widely accepted theory is the sliding anal canal lining theory, which suggests that hemorrhoids develop when the supporting tissues of the anal cushions deteriorate or degenerate. Hemorrhoids are the pathological term for the abnormal downward displacement of the anal cushions, resulting in venous dilatation.[1,6]

Pathological changes associated with hemorrhoids:[1]

- Anomalous venous dilatation
- Vascular thrombosis
- Degeneration in the collagen fibers and fibroelastic tissues
- Distorted and ruptured anal subepithelial muscle
- Inflammation
- Mucosal ulceration
- Ischemia.

Grading of hemorrhoids

Hemorrhoids are classified based on their location in relation to the dentate line—the junction between columnar and squamous epithelium—and the degree of prolapse. This classification helps in selecting and comparing treatment options. Following is the classification:[1,6]

- Internal hemorrhoids: Originating above the dentate line and covered by anal mucosa
- External hemorrhoids: Originating below the dentate line and covered by squamous epithelium
- Mixed hemorrhoids: Extending both above and below the dentate line.

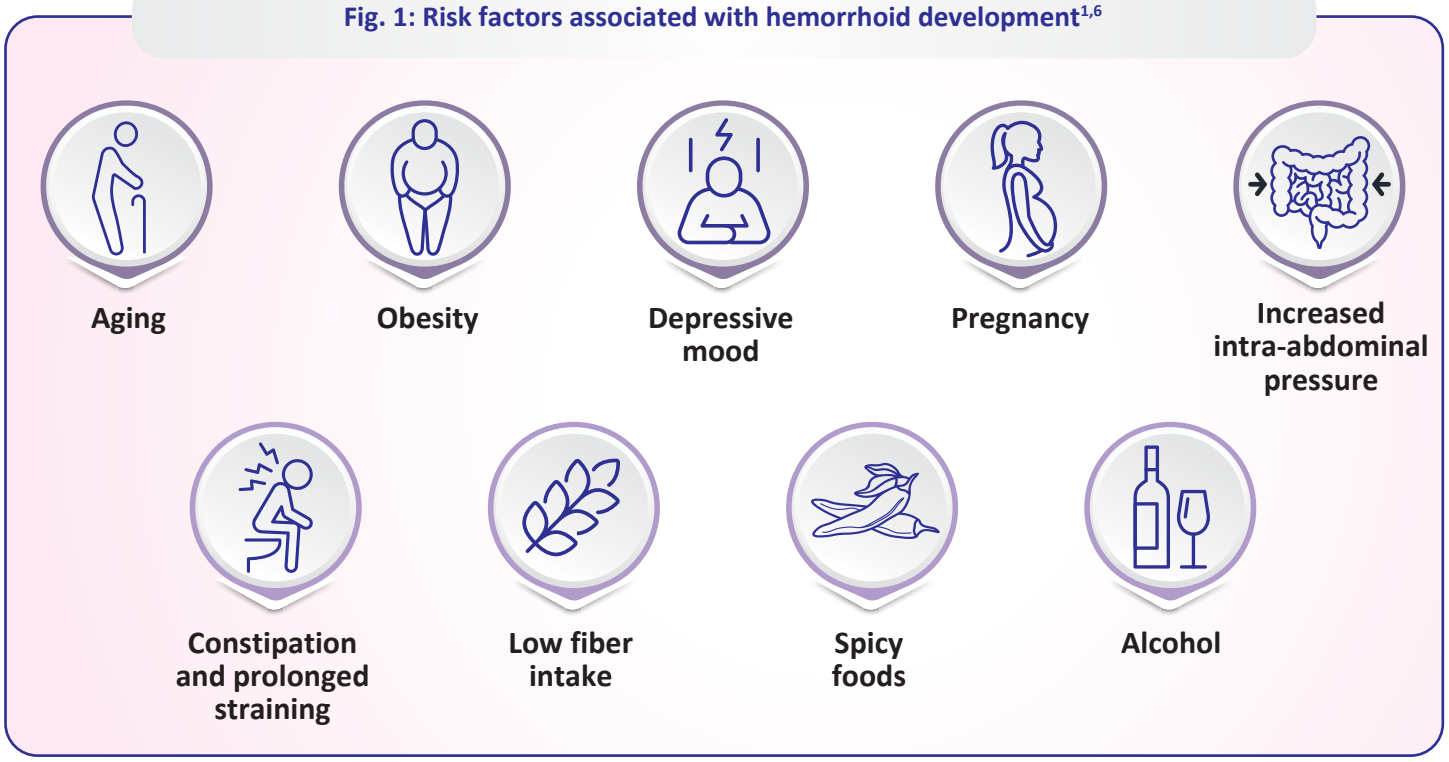
Internal hemorrhoids are further graded by the Goligher classification system (Table 1):[1,6]

Table 1: Classification of internal hemorrhoids	
Grade	**Description**
I (First degree hemorrhoids)	• Bleeding but non-prolapsing hemorrhoids
II (Second degree hemorrhoids)	• Hemorrhoids prolapse on straining but reduce spontaneously
lll (Third degree hemorrhoids)	• Hemorrhoids prolapse on straining or exertion • Require manual reduction
IV (Fourth degree hemorrhoids)	• Permanent prolapsing hemorrhoids • Non-reducible

Risk factors and presentation

Several risk factors contribute to hemorrhoid development, including aging, obesity, depressive mood, and pregnancy (Fig. 1). Amplified intra-abdominal pressure from prolonged straining and constipation compromises venous drainage in the hemorrhoid plexus, leading to hemorrhoid formation.[6] Straining triggers symptoms such as bleeding and prolapse, especially in individuals with a history of hemorrhoids.[1] Pregnancy often causes anal cushion congestion and symptomatic hemorrhoids, which usually resolve after childbirth. Dietary factors, including low fiber intake, spicy foods, and alcohol, may also play a role in exacerbating symptoms, though evidence is varying. Some reports suggest that diarrhea may contribute to hemorrhoid development.[1]

Fig. 1: Risk factors associated with hemorrhoid development[1,6]

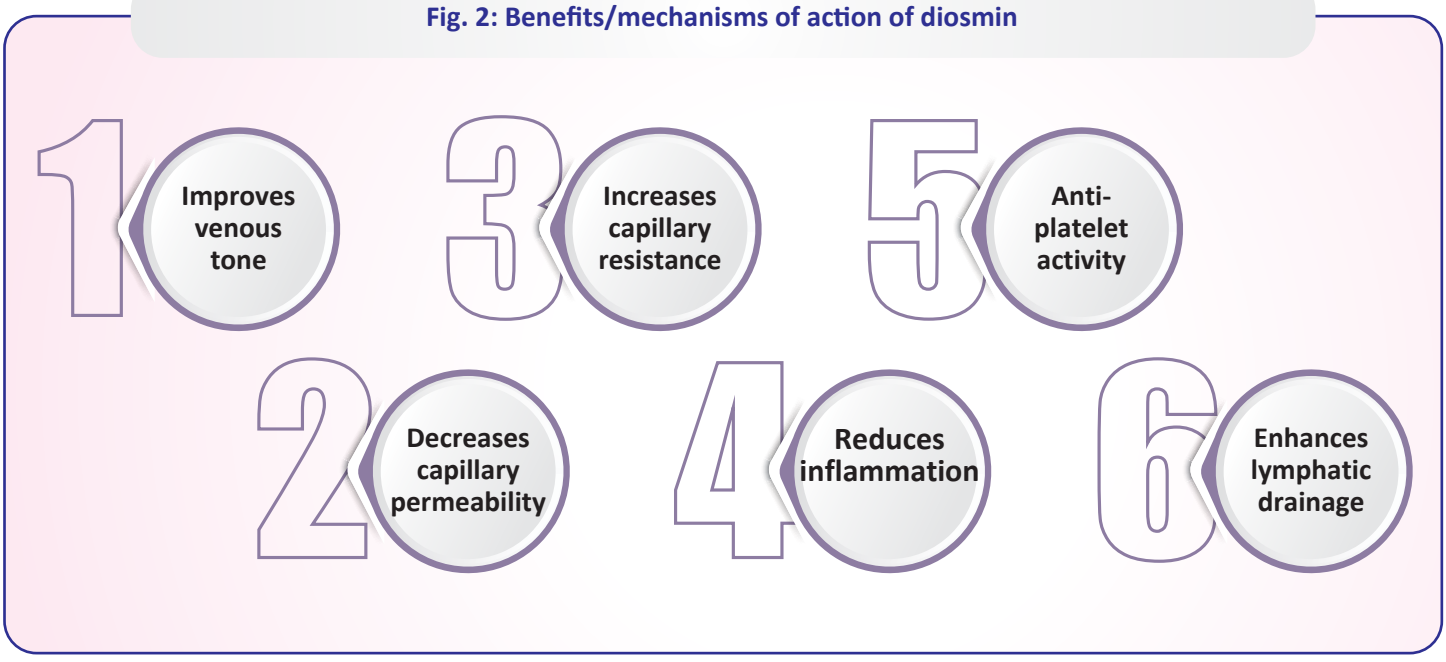


Role of diosmin in management of hemorrhoids

Diosmin has been used worldwide for over 30 years as a phlebotonic and vascular-protecting agent, demonstrating a good safety and efficacy profile. As a flavonoid, diosmin offers additional benefits such as anti-inflammatory, free radical scavenging, and anti-mutagenic actions. Clinically, diosmin has been employed to manage variceal dilatations like hemorrhoids, as well as chronic venous insufficiency, lymphedema, and varicose veins.[7] Diosmin works by inhibiting the breakdown of noradrenaline. It helps reduce inflammation, inhibit platelet function, and enhance lymphatic drainage.[7,8] Its micronized form boosts its bioavailability and effectiveness.[9,10]

Fig. 2 depicts the proposed benefits of diosmin.[7,8,11]

Fig. 2: Benefits/mechanisms of action of diosmin



Clinical evidence showing efficacy of diosmin in hemorrhoid treatment

1. IMPROVED SYMPTOM SCORES:

A two-month treatment with micronized purified diosmin significantly reduced the frequency and severity of acute hemorrhoidal attacks compared to placebo.[12]

Key study outcomes:[12]

- With diosmin, 40% of the patients experienced an attack with a mean duration of 2.6 days and severity score of 1.1.
- Placebo resulted in 70% of patients with attacks with mean duration of 4.6 days and a severity score of 1.6.
- Overall symptom scores improved significantly with diosmin (from 6.6 to 1.1) compared to placebo (from 6.1 to 4.0; Fig. 3).

2. REDUCTION IN PAIN AND BLEEDING:

A study evaluated the role of purified diosmin in 66 patients with grade I-IV hemorrhoids.

Key study outcomes (Fig. 4):[13]

- Diosmin reduced pain by 79% in the first week and 98% in the second week.
- Bleeding decreased by 67% in the first week and 86% in the second week.
- Diosmin exhibited excellent tolerability.

Fig. 3: Reduction in symptom score with micronized purified disomin and placebo in patients with hemorrhoidal disease

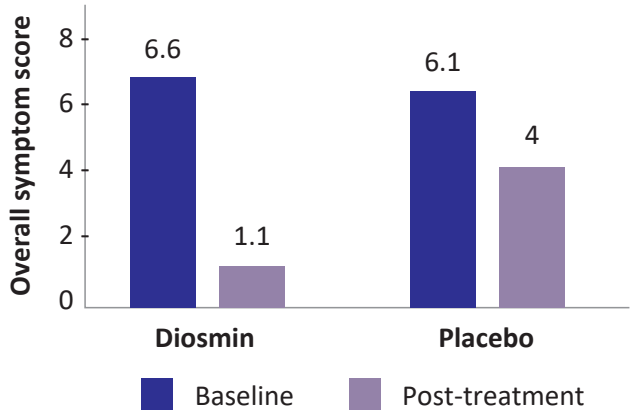
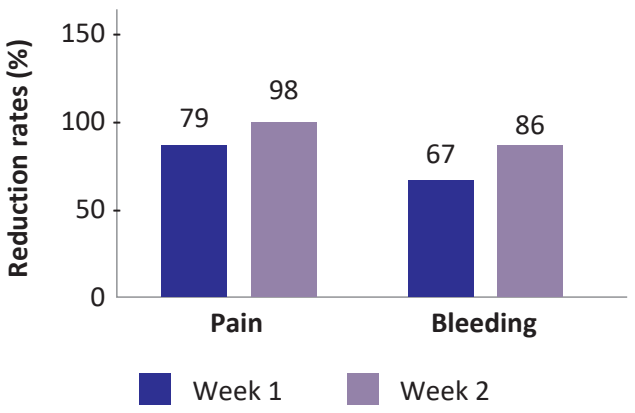


Fig. 4: Efficacy of diosmin therapy in reducing pain and bleeding in patients with hemorrhoids



3. LESSENED PAIN INTENSITY:

A systematic review of clinical trials assessed the effectiveness of diosmin on pain after hemorrhoidectomy. Four high-quality randomized clinical trials involving 824 patients were included, with pain intensity measured using the Visual Analog Scale. Diosmin was administered at doses of 500 mg in three studies and 300 mg in one study. Results showed that three studies reported a **reduction in pain intensity with diosmin.** Diosmin appears to reduce pain intensity following hemorrhoidectomy.[14]

4. SHORTER STAY IN THE HOSPITAL:

Another study evaluated the effect of diosmin in managing post-hemorrhoidectomy symptoms in 86 patients who were randomized to receive either diosmin for one week or a placebo. The study assessed pain, bleeding, heaviness, pruritus, wound edema, and mucosal discharge following surgery, along with postoperative symptoms and hospitalization time. Results showed a statistically significant improvement in pain, heaviness, bleeding, and pruritus from baseline to the eighth week post-operation in the diosmin group. Additionally, patients who received **diosmin had a shorter median hospital stay (6.1 days)** compared to the control group (7.3 days), a **faster median time to first bowel action (48 hours vs. 56 hours), and fewer bowel actions in the first week (9 vs. 14).**[15]

Advantages of 100% pure micronized diosmin

The use of 100% pure micronized diosmin is advantageous for hemorrhoid treatment due to its improved absorption and bioavailability, as it avoids the interference of other flavonoids that can reduce tissue absorption and distribution. For therapy, choosing the purest form of diosmin (100% pure) is a must.

Diosmin is isolated/extracted from the flavonoid hesperidin.[7] Diosmin-containing products are available which may be in combination with hesperidin impurity [Diosmin+Hesperidin, referred as micronized purified flavonoid fraction (MPFF)].[16] Impurities may be associated with reduced clinical effects and with side effects.

As per British Pharmacopoeia, only diosmin is considered as the main therapeutic agent, while hesperidin is considered an impurity, whose amount should not exceed beyond 4%. US Pharmacopeia has suggested the upper limit of hesperidin as 5%.[17,18] In India, 100% pure diosmin is available.[19]

Therefore, it seems prudent to use purified and micronized diosmin, without impurities like hesperidin, for managing hemorrhoids.

Conclusion

Diosmin stands out as a highly effective and safe therapeutic agent for the management of hemorrhoids, offering a multifaceted approach that addresses the core pathophysiological aspects of the condition. By improving vascular tone, reducing inflammation, and improving lymphatic drainage, diosmin not only alleviates the acute symptoms of hemorrhoids but also reduces the frequency and severity of attacks. Clinical evidence robustly supports its efficacy in diminishing pain, bleeding, and the necessity for surgical interventions, thereby significantly enhancing patient outcomes. Its superior bioavailability in micronized form further underscores its therapeutic potential. Given the substantial benefits and favorable safety profile, diosmin represents a compelling option for the comprehensive management of hemorrhoids, providing relief and improving the quality of life for millions affected by this condition.

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