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REVIEW ARTICLE

The Use of Diosmin in the Treatment of Surgical Conditions: Hemorrhoids and Chronic Venous Insufficiency

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ABSTRACT

Diosmin, a flavonoid compound, has been extensively studied for its therapeutic potential in managing vascular conditions, such as hemorrhoids and chronic venous insufficiency. This paper reviews the historical development and clinical evidence supporting the use of diosmin in both conservative and non-surgical treatments of these conditions. Diosmin's phlebotonic and anti-inflammatory properties contribute to symptom relief by enhancing venous tone, reducing edema, and alleviating pain. Clinical studies highlight its effectiveness in treating symptoms of hemorrhoids, including pain, bleeding, and anal discomfort, and in improving venous health in patients with chronic venous insufficiency, such as reducing leg swelling and improving skin changes. In addition, diosmin's ability to enhance the effects of other conservative treatments, such as local therapies for hemorrhoids or compression therapy for chronic venous insufficiency, may reduce the need for surgical interventions. This paper emphasizes diosmin's role as an adjunct to conservative management, potentially delaying or preventing surgery, improving patient outcomes, and enhancing quality of life. The evidence suggests that diosmin is a valuable tool in the non-surgical treatment of these common vascular conditions.

Keywords: Diosmin, evidence-based expert opinion, therapeutic potentials

INTRODUCTION

Diosmin (diosmetin 7-O-rutinoside), a benzopyrone and flavone glycoside derived from hesperidin, a flavanone found in citrus fruits, has been produced and studied since the 1950s. Diosmin is a phlebotonic dietary supplement known for its beneficial effects in treating conditions, such as hemorrhoids and chronic venous insufficiency, including varicose veins, spider veins, leg edema, stasis dermatitis, and venous ulcers.[1-4]

HISTORICAL BACKGROUND AND EARLY STUDIES ON DIOSMIN

In 1971, de Tourris *et al.* first explored the use of diosmin in the treatment of heavy leg syndrome, which commonly occurs during menopause.[3] Two years later, Muller *et al.* highlighted the potential of Daflon (a preparation containing 450 mg diosmin and 50 mg hesperidin) in treating various obstetrical and gynecological conditions.[4] The efficacy of diosmin in the management of venous insufficiency was further supported in studies from the early 1970s by Van Gysel and Veroft, and Peeters, who recognized its therapeutic potential in patients with venous insufficiency and proctologic conditions, respectively.[5,6]

In 1973, Berson suggested a potential therapeutic value of diosmin in the treatment of varicose veins.[7]

In 1980, Natili *et al*. reported the use of Daflon for the treatment and prevention of arteriovenous fistulas' complications during chronic hemodialysis patients.[8]

Further studies in the 1980s reinforced diosmin's value. Notably, in 1988, Duchene Marullaz *et al*. reviewed placebo-controlled trials and concluded

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that a single dose of Daflon 500 mg (450 mg diosmin and 50 mg hesperidin) improved chronic venous insufficiency symptoms, with optimal results achieved at 1000 mg daily.[9]

Similarly, a placebo-controlled study by Laurent *et al*. in 1988 demonstrated significant improvement in both clinical symptoms and venous hemodynamics in patients with chronic venous insufficiency after 2 months of treatment with Daflon 500 mg twice daily.

The study included 200 patients (174 females, 26 males) with chronic venous insufficiency, including 83 patients having organic causes, and 117 patients having functional venous insufficiency. In addition to marked symptomatic improvement, plethysmographic parameters showed marked improvement in venous hemodynamics.[10]

DIOSMIN IN THE TREATMENT OF HEMORRHOIDS

Hemorrhoids, a common condition affecting the anal region, can lead to considerable discomfort. In 1988, Tajana *et al*. from Italy observed marked improvement in edema and erythema in patients with hemorrhoids treated with diosmin ointment.

They described the treatment of fifty patients (17 females and 33 males) who had hemorrhoids (Grade 1, 2, 3, or 4) with diosmin ointment. Treatment was associated with improvement in edema and erythema.[11]

This was followed by further studies demonstrating diosmin's ability to improve symptoms of acute hemorrhoids, such as pain, bleeding, and anal discomfort.

For instance, a placebo-controlled study by Cospite from Italy in 1994 found that treatment with Daflon 500 mg was associated with more rapid improvement of symptoms of acute hemorrhoids, especially proctorrhagia and anal pain.

Cospite reported a placebo-controlled study which included 100 patients with acute hemorrhoids presenting with proctorrhagia, anal discomfort, pain, and anal discharge. Fifty patients received a placebo, and 50 patients were treated with Daflon 500 mg (3 tablets twice daily for 4 days followed by two tablets twice daily for 3 days). Treatment was associated with more rapid improvement of the symptoms of acute hemorrhoids.[12]

In 1992, Thanapongsathorn and Vajrabukka reported a placebo-controlled study which included 100 patients who had acute symptoms of internal hemorrhoids (1st-degree and 2nd-degree) who had been treated conservatively with a bulk laxative. Fifty patients received Daflon and fifty patients received a placebo. Two weeks of treatment were associated with marked symptomatic improvement.[13]

In 2018, Bashankaev from Russia and his American colleagues recommended the use of diosmin treatment of hemorrhoids bases on a Cochrane review of 24 controlled involving 2,334 patients. They emphasized the complexity of hemorrhoids treatment and the need for combination therapy.[14]

In 2016, Lorenc and Gökçe from Poland reviewed the available evidence provided by 18 studies and recommend the use of tribenoside plus lidocaine suppository or rectal cream (Procto-Glyvenol) for the local treatment of hemorrhoids.[15]

Therefore, based of the notion of Bashankaev *et al*. who emphasized the need for combination therapy, and the evidence provided by Lorenc and Gökçe, the non-surgical treatment of hemorrhoids can be improved by combing oral diosmin and local procto-glyvenol therapy.[14,15]

In 2020, Sheikh conducted a systematic review and meta-analytic study involving 11 studies. The study found that when Daflon was used in the treatment of hemorrhoids, it improved pain, bleeding, anal discharge/leakage, pruritus, and tenesmus.[16]

DIOSMIN IN CHRONIC VENOUS INSUFFICIENCY

Chronic venous insufficiency is a condition characterized by impaired venous return and is commonly associated with symptoms, such as leg pain, swelling, and ulcers. Early studies by Guillot *et al*. from France in 1989[17] and Tsouderos in 1993[18] demonstrated that oral Daflon 500 mg led to significant symptomatic improvement in chronic venous insufficiency, including reductions in edema, calf circumference, and venous distensibility. In addition, a placebo-controlled study by Geroulakos and Nicolaides from England

in 1994.[19] emphasized the non-surgical potential of Daflon, with patients showing symptomatic relief and improved venous tone following treatment.

Guillot *et al*. described the treatment of 170 patients who had chronic venous insufficiency with oral Daflon 500 mg, twice daily. Treatment was associated with marked improvements in functional discomfort, supra-malleolar circumference, and calf circumference. Seven patients complained of stomach pain. Guillot *et al*. considered treatment to be effective and safe.[17]

Tsouderos reported a study that included twenty patients who developed post-thrombotic syndrome treated with oral Daflon 500 mg. Treatment was associated with a reduction of venous capacity ($P < 0.001$), venous distensibility ($P < 0.001$), and venous outflow time ($P < 0.001$). Tsouderos also reported that the treatment of two parallel groups of twenty patients who had functional chronic venous insufficiency with oral Daflon 500 mg. Compared to placebo 1 month and 2 months treatments were associated with symptomatic improvement and reduction of edema occurring in association with increased venous tone.[18]

Geroulakos and Nicolaides reported a placebo-controlled study that included patients who had chronic venous insufficiency. 183 patients received Daflon 500 mg and 183 patients received a placebo. Treatment was associated with a reduction in venous distensibility and symptomatic improvement with a reduction of supramalleolar circumference. Side effects were rare and only three patients stopped treatment because of side effects.[19]

In 2006, Savel'ev *et al*. from Russia conducted a meta-analytic study of five studies involving 723 patients. The study showed that patients having chronic venous insufficiency complicated by venous trophic ulcers treated by micronized diosmin benefited from the favorable effect of diosmin on middle-sized trophic ulcers (5–10 cm).[20]

In 2018, Kakkos and Nicolaides conducted a systematic review and meta-analytic study involving seven placebo-controlled with 1,692 patients with chronic venous disease. The study showed that Daflon markedly improved leg symptoms and signs, including pain, heaviness, feeling of swelling, cramps, paresthesia, pruritus, burning sensation, leg redness, skin changes, and ankle circumference. The authors concluded that high-quality evidence is available supporting the effectiveness of Daflon in improving leg edema and leg symptoms, and also the quality of life of the treated patients.[21]

DIOSMIN IN VASCULAR AND PREMENSTRUAL MASTODYNIA

In 1990, Meggiorini *et al*. reported a study that included 240 patients who had vascular and premenstrual mastodynia. 120 patients were treated with synthetic diosmin for 1 year, and 120 patients served as controls. Treatment was associated with marked symptomatic improvement.[22]

DIOSMIN IN SYMPTOMATIC CAPILLARY FRAGILITY

In 1993, Galley and Thiollet from France reported a placebo-controlled study that included 100 patients who had symptoms of capillary fragility, including spontaneous ecchymosis, epistaxis, purpura, petechiae, gingivorrhagia, metrorrhagia, and conjunctival hemorrhage. Six weeks of treatment with Daflon was associated with marked symptomatic improvement.[23]

DIOSMIN AND CONSERVATIVE MANAGEMENT

Diosmin has shown promise as an adjunct to conservative treatment, particularly in the management of conditions that might otherwise require surgical intervention. By improving venous tone, reducing inflammation, and alleviating symptoms, such as pain, heaviness, and edema, diosmin can potentially delay or prevent the need for invasive procedures.

In the case of hemorrhoids, combining oral diosmin with local treatments, such as Procto-Glyvenol (a topical cream containing tribenoside and lidocaine), can enhance treatment outcomes and provide more rapid symptom relief, reducing the need for surgical intervention in patients with acute hemorrhoids.[11-16]

Similarly, in the context of chronic venous insufficiency, diosmin may reduce the progression of the disease, thus preventing or delaying the need for surgical options, such as sclerotherapy or vein stripping.

As demonstrated by studies, such as those by Kakkos and Nicolaides, diosmin significantly improves symptoms of chronic venous insufficiency, including pain, leg swelling, and skin changes, thereby improving patients' quality of life and reducing the necessity for more invasive interventions.[21]

MECHANISMS OF ACTION AND EFFECTIVENESS

Diosmin exerts its effects primarily through its phlebotonic and anti-inflammatory properties. It enhances venous tone by increasing vascular smooth muscle contraction and improving lymphatic drainage. In addition, diosmin has anti-edematous effects, reducing fluid retention in the tissues. These actions collectively contribute to the relief of symptoms, such as leg swelling, pain, and discomfort in conditions, such as hemorrhoids and chronic venous insufficiency. Moreover, diosmin's antioxidant properties help in reducing vascular inflammation and promoting better venous health, which further contributes to its effectiveness in managing these conditions.[11-21]

CONCLUSION

The evidence supporting the use of diosmin in the treatment of hemorrhoids and chronic venous insufficiency is robust, with numerous studies confirming its efficacy in alleviating symptoms and improving venous health.

Diosmin's role in conservative treatment is especially significant, as it offers a non-invasive alternative to surgery. By improving symptoms and enhancing venous function, diosmin can reduce the need for surgical intervention, particularly in patients with mild to moderate forms of hemorrhoids or chronic venous insufficiency.

CONFLICT OF INTEREST

None.

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