a fórmula

TROXERRUTINA

FLAVONOIDE DERIVADO DA RUTINA DE AÇÃO ANTIVARICOSA

Estudos

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a fórmula

TROXERRUTINA

Flavonoide derivado da rutina de ação antivaricosa

DESCRIÇÃO

A **Troxerrutina** é um flavonoide derivado da rutina (tri-hidroxietilrutina) com efeito antivaricoso.

MECANISMO DE AÇÃO

A **Troxerrutina** apresenta efeito protetor do endotélio capilar melhorando a circulação sanguínea por efeitos hemodinâmicos e antitrombóticos, reduzindo a exsudação do plasma ao interstício, evitando a formação de edemas inflamatórios locais, inclusive na vasoconstrição, e normalizando tanto o fluxo sanguíneo como linfático ao melhorar a microcirculação. Já na insuficiência venosa crônica, a **Troxerrutina** diminui a adesão de leucócitos (que agridem as paredes capilares e causam inflamações), assim como reduz a agregação de trombócitos (relacionado com vários processos patológicos).
Estudos recentes indicam a capacidade da **troxerrutina** em inibir a sinalização de NF-kB, que desempenha papel importante na formação das dores neuropáticas, além de ativar a via AMPK / SIRT-1, exercendo efeito anti-inflamatório.

INDICAÇÕES

- ✓ Edemas inflamatórios;
- ✓ Varizes; Sintomas de hemorroida;
- ✓ Circulação sanguínea e linfática; Insuficiência cardíaca crônica.

DOSE USUAL

Recomendação oral de 0,5 a 1 g de **Troxerrutina** ao dia. Recomendação tópica de 1 a 2% ao dia.

SUGESTÕES DE FÓRMULAS

Troxerrutina..... 90mg
Cumarina.....15mg

Modo de uso: 1 dose, 3 vezes ao dia.
Indicação: diminuição de edemas locais; melhorar a microcirculação.

Troxerrutina.....2%
Tintura de Arnica *(Arnica montana)*.....5%
Extrato glicólico de Cavalinha (*Equisetum arvense* L).....3%
Loção Aristoflax qsp.....100ml

Modo de uso: aplicar 1 a 2 vezes ao dia, massageando continuamente.
Indicação: microvarizes, contusões e hematomas.

Troxerrutina..... 300mg
Hesperidina..... 300mg
Diosmina..... 300mg
Vitamina C..... 12mg

Modo de uso: 1 dose ao dia.
Indicação: controle de edema e trombos; sintomas de hemorroida.

Troxerrutina.....2%
Escina beta.....0,4%
Extrato glicólico de Arnica *(Arnica montana)*.....2%
Gel qsp.....100g

Modo de uso: aplicar 1 a 2 vezes ao dia, massageando continuamente.
Indicação: microvarizes, contusões e hematomas.

PRINCIPAIS REFERÊNCIAS

VANSCHEIDT, W. et al. The efficacy and safety of a coumarin-/troxerutin combination (SB-LOT) in patients with chronic venous insufficiency: A double blind placebo controlled randomised study. **Vasa**, v. 31, n. 3, p. 185-190, 2002. Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/12236023>. Acesso em: 29 de janeiro de 2018.

GIANNINI, I. et al. Flavonoids mixture (diosmin, troxerutin, hesperidin) in the treatment of acute hemorrhoidal disease: a prospective, randomized, triple-blind, controlled trial. **Techniques in coloproctology**, v. 19, n. 6, p. 339-345, 2015. Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/25893991>. Acesso em: 29 de janeiro de 2018.

TROXERRUTINA

ESTUDOS CLÍNICOS

Flavonoids mixture (diosmin, troxerutin, hesperidin) in the treatment of acute hemorrhoidal disease: a prospective, randomized, triple-blind, controlled trial.

BACKGROUND: The role of a mixture of phlebotonics in the treatment of acute hemorrhoid crisis is investigated to test their efficacy. METHODS: One hundred and thirty-four consecutive patients with an acute hemorrhoidal crisis recruited in five colorectal units entered the study. Sixty-six of them were randomized to receive a mixture of diosmin, troxerutin and hesperidin (group A), and 68 a placebo (group B). The main symptoms, the use of oral painkillers and the Bristol scale score were recorded at each scheduled visit and compared using both Student's t test for independent samples and the ANOVA models for repeated measures. The presence of edema, prolapse and thrombosis were also recorded and compared using the Chi-square test. Furthermore, the trend of proportions during the time of the evaluations was assessed by the Chi-square test for linear trend. RESULTS: Pain, bleeding and the proportion of patients who reported persistence of edema and thrombosis decreased significantly after 12 days of treatment in group A. After 6 days, the number of paracetamol tablets taken by patients in group A was significantly lower than the amount of flavonoid mixture. CONCLUSIONS: The use of a mixture of diosmin, troxerutin and hesperidin is a safe and effective mean of managing symptoms of acute hemorrhoidal disease. Furthermore, in patients receiving treatment, there was faster control and lower persistence of edema and thrombosis.

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Involvement of AMPK/SIRT1 pathway in anti-allodynic effect of troxerutin in CCI-induced neuropathic pain.

Neuropathic pain was regarded as a main form of chronic pain condition that remains difficult to treat. Conventional pharmacotherapy for neuropathic pain responsed vary and side effects limited their compliance. These prompted us to find new alternatives. In this study, we investigated the effect of troxerutin on treatment of CCI-induced neuropathic pain. Results showed that troxerutin significantly reversed mechanical allodynia and thermal hyperalgesia. In L4-6 spinal cord, troxerutin reduced the expression of INF-γ, IL-1β, TNF-α, and activation of NF-κB(p65). Immunofluorescence results showed that troxerutin significantly inhibited microglia activation induced by CCI surgery. Further, troxerutin treatment significantly induced AMPK activation and inhibited CCI-induced SIRT1 decrease. However, AMPK inhibitor compound C and SIRT1 inhibitor EX527 inhibited analgesic effect of troxerutin in CCI mice. This demonstrated the involvement of AMPK/SIRT1 pathway in anti-allodynic effect of troxerutin in CCI mice. Troxerutin could be developed as a potential therapeutic agent for neuropathic pain.

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Troxerutin, a mixture of O-hydroxyethyl derivatives of the natural flavonoid rutin: Chemical stability and analytical aspects.

Troxerutin (TRX) is a mixture of semisynthetic hydroxyethylrutosides (Hers) arising from hydroxyethylation of rutin, a natural occurring flavonoid. TRX is commonly used for its anti-oxidant and anti-inflammatory properties in chronic venous insufficiency and other vascular disorders. In recent studies, the protective effects of TRX in Alzheimer's disease, colon carcinogenesis and hepatocellular carcinoma are emerged. However, the chemical stability of TRX has never been studied. Hence, the aims of the work were to study the TRX chemical stability through a forced degradation study and to develop and validate a new stability indicating LC-UV method for determination of TRX. In order to perform the study, TRX stability was tested in various stress conditions analysing the degradation samples by LC-MS. Three degradation products (DPs; D1, D2 and D3, 3',4',7-Tri-O-(β-hydroxyethyl)quercetin, 3',4',5,7-Tetra-O-(β-hydroxyethyl)quercetin and 3',4'-Di-O-(β-hydroxyethyl)quercetin respectively) arising from degradation in acidic conditions were identified and synthesized: among them, D1 resulted the stability indicator for hydrolytic degradation. Furthermore, a stability-indicating LC-UV method for simultaneous determination of triHer (3',4',7-Tri-O-(β-hydroxyethyl)rutin, the principal component of the mixture) and D1 was developed and validated. The LC-UV method consisted in a gradient elution on a Phenomenex Kinetex EVO C18 (150 × 3 mm, 5 µm) with acetonitrile and ammonium bicarbonate buffer (10 mM, pH 9.2). The method was linear for triHer (20-60 µg mL-1) and D1 (5.1-35 µg mL-1). The intraday and interday precision were determined and expressed as RSDs: all the values were ≤ 2% for both triHer and

D1. The method demonstrated also to be accurate and robust and the average recoveries were 98.8 and 97.9% for triHer and D1, respectively. Moreover, the method resulted selective and specific for all of the components present in the degradation pattern of TRX (diHer (3',4'-Di-O-(β-hydroxyethyl)rutin), triHer, tetraHer (3',4',5,7-Tetra-O-(β-hydroxyethyl)rutin), D3, D1 and D2) and it was successfully applied for the stability studies of both drug substances and drug products.

Antifatigue effects of troxerutin on exercise endurance capacity, oxidative stress and matrix metalloproteinase-9 levels in trained male rats.

The aim of this study was to investigate effects of troxerutin (TRX) on endurance capacity, oxidative stress and matrix metalloproteinase-9 (MMP-9) levels in trained male rats. Forty male Wistar rats were divided into five groups. The control (Vehicle) and exercise training (5 days/week) with vehicle treatment (Exercise), exercise training with TRX treatment at 75 (Ex-TRX75), 150 (Ex-TRX150), and 300 mg/kg (Ex-TRX300). The treated groups received TRX by gavage every day while the other groups received water for 30 days. On the 30th day, rats were sacrificed immediately after exhaustive swimming test, and some biochemical parameters were measured. Exhaustion swimming time in the Ex-TRX75, Ex-TRX150 and Ex-TRX300 groups significantly increased 1.2-, 1.93- and 2.1-fold compared to the vehicle group, respectively. TRX significantly increased glucose level ($P < 0.05$) and reduced creatine kinase activity ($P < 0.001$) compared to the vehicle and exercise groups. TRX300 significantly reduced alkaline phosphatase and lactate dehydrogenase activities ($P < 0.05$) and blood urea nitrogen ($P < 0.05$) and MMP-9 levels ($P < 0.05$) compared to the vehicle and exercise groups. Additionally, TRX300 and TRX150 significantly increased superoxide dismutase activity compared to the vehicle group ($P < 0.05$). Our results provide experimental evidence in supporting clinical use of TRX as an effective agent against fatigue.

Comparison of the effects of troxerutin and heparinoid on flap necrosis.

We aimed to assess the effects of local troxerutin and heparinoid (HEP) treatments in a model of flap necrosis. Three groups of Wistar albino rats, each comprising 10 animals were used. A cranially based 6x3-cm full-thickness random-pattern skin flap was raised and sutured to the same area in each model. The control group was treated daily with normal saline, the second with topical HEP and the third with topical troxerutin. The amount of flap necrosis was measured in all groups by the end of the seventh day. Flap tissues were excised for histological analysis and evaluation of the expression of vascular endothelial growth factor (VEGF) levels. Assessment of the blood levels of nitric oxide was also performed in each animal by cardiac puncture. The mean area of flap necrosis was 110.6mm(2) in the control, 39.44 mm(2) in the troxerutin and 47.11 mm(2) in the heparinoid-treated rats. The treatment arms exhibited significant reduction in areas of flap necrosis, compared with the control group ($p<0.001$), but it was similar among treatment groups ($p=0.60$). The rates of fibroblast proliferation were decreased in control group as compared to HEP and troxerutin arms ($p<0.001$). The mean level of collagen density, collagen organisation, granulation tissue and demarcation were similar in all rats. Measurement of VEGF expression did not show any significant difference between the groups ($p=0.30$). Nitric oxide levels were significantly higher in control rats, as compared to treatment groups ($p<0.0001$), but were similar in treatment arms ($p=0.45$). Our results suggest that troxerutin and HEP effectively reduce the flap necrosis and improve flap survival. The observed effects might be due to their anti-oedematogenic, radical-scavenging, antioxidant effects and supportive activities on capillary permeability and transudation.

The efficacy and safety of a coumarin-/troxerutin-combination (SB-LOT) in patients with chronic venous insufficiency: a double blind placebo-controlled randomised study.

BACKGROUND: The objective was to evaluate the oedema-protective effect of a vasoactive drug (coumarin/troxerutin [SB-LOT]) plus compression stockings in patients suffering from chronic venous insufficiency after decongestion of the legs as recommended by the new guidelines. PATIENTS AND METHODS: 231 patients were randomly assigned medical compression stockings plus SB-LOT (90 mg coumarin and 540 mg troxerutin per day) or medical compression stockings plus placebo for the first 4 weeks and SB-LOT or placebo for the second 12 weeks of the study. The primary efficacy endpoint was the lower leg volume measured by well-established water plethysmometry. RESULTS: 226 patients were evaluated. After ceasing compression stockings, an edema protective effect was detected in the SB-LOT-group but not in the controls. Recurrence of leg volume increase was by 6.5 +/- 12.1 ml and by 36.7 +/- 12.1 ml in the SB-LOT and placebo group, respectively (p = 0.0402). The local complaint score and general aspects of quality of life were also superior for the SB-LOT-group (p = 0.0041). Significant differences were also observed with regard to clinical global impression and therapeutic effect. No serious adverse drug reaction or clinically relevant impairment of laboratory parameters occur. CONCLUSION: This study confirms the oedema-protective effect of SB-LOT in chronic venous insufficiency and provides a treatment option for patients who discontinue compression after a short time.

REFERÊNCIAS

GIANNINI, I. et al. Flavonoids mixture (diosmin, troxerutin, hesperidin) in the treatment of acute hemorrhoidal disease: a prospective, randomized, triple-blind, controlled trial. **Techniques in coloproctology**, v. 19, n. 6, p. 339-345, 2015. Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/25893991>. Acesso em: 29 de janeiro de 2018.

GUI, Yulong et al. Involvement of AMPK/SIRT1 pathway in anti-allodynic effect of troxerutin in CCI-induced neuropathic pain. **European journal of pharmacology**, v. 769, p. 234-241, 2015. Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/26601804>. Acesso em: 29 de janeiro de 2018.

BIANCHI, Michele et al. Troxerutin, a mixture of O-hydroxyethyl derivatives of the natural flavonoid rutin: Chemical stability and analytical aspects. **Journal of pharmaceutical and biomedical analysis**, v. 150, p. 248-257, 2018. Disponível em: < https://www.sciencedirect.com/science/article/pii/S0731708517322744>. Acesso em: 29 de janeiro de 2018.

ZAMANIAN, Mohammad et al. Antifatigue effects of troxerutin on exercise endurance capacity, oxidative stress and matrix metalloproteinase-9 levels in trained male rats. **Fundamental & clinical pharmacology**, v. 31, n. 4, p. 447-455, 2017. Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/28214375>. Acesso em: 29 de janeiro de 2018.

VANSCHEIDT, W. et al. The efficacy and safety of a coumarin-/troxerutin combination (SB-LOT) in patients with chronic venous insufficiency: A double blind placebo controlled randomised study. **Vasa**, v. 31, n. 3, p. 185-190, 2002. Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/12236023>. Acesso em: 29 de janeiro de 2018.

CELIK, Alper et al. Comparison of the effects of troxerutin and heparinoid on flap necrosis. **Journal of Plastic, Reconstructive & Aesthetic Surgery**, v. 63, n. 5, p. 875-883, 2010. Disponível em: < https://www.ncbi.nlm.nih.gov/pubmed/19346174>. Acesso em: 29 de janeiro de 2018.