

PADMA 28

SCIENTIFIC DOCUMENTATION

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Peripheral Arterial Occlusive Disease, PAOD

Melzer J, Brignoli R, Diehm C, Reichling J, Do DD, Saller R

Treating intermittent claudication with Tibetan medicine Padma 28: Does it work?

Artherosclerosis 2006, 189:39-46.

Herbal drugs are being increasingly used in medical practice, often without appropriate scrutiny of their safety and efficacy. The medicinal product Padma 28 is a fixed combination with Tibetan origin, used in Europe since the 1960s for the symptomatic treatment of circulatory disorders, including those of peripheral arterial occlusive disease (PAOD). We have conducted an analysis of all available data on this herbal drug from published literature as well as from original data we obtained from contacting the authors of published papers, reports and the manufacturer. A total of 19 trials have reported on 2084 patients to date, 444 of whom were in six controlled clinical studies on PAOD. A meta-analysis of five trials showed Padma 28 to increase walking distance by >100m in 18.2% of the patients with verum, versus 2.1% with placebo ($P < 0.001$; odds ratio: 10 [95% CI 3.03, 33.33]; RR: 0.12; number needed to treat=6.2). The safety profile appears to be favourable. Available evidence shows that Padma 28 provides significant relief from PAOD-related symptoms (i.e. walking distance), probably of the same order of magnitude as other employed medications. However, larger confirmatory RCTs are desirable.

Keywords: Peripheral arterial occlusive disease (PAOD), Maximum walking distance, Tibetan herbal drug, Phytotherapy, Meta-analysis, CAM, Padma 28

Hepatitis B

Brzosko WJ, Jankowski A

PADMA 28 in patients with chronic hepatitis B: Clinical and immunological effects

Schweiz Zschr für GanzheitsMedizin 1992;(7/8 Suppl 1):13-4.

Since our first studies on the localization of the antigens (Hbs Ag, Hbc Ag) of the hepatitis B virus (HBV) there is now agreement that the inflammatory damage to the liver through chronically active hepatitis B (CAH-B) is not the direct result of the virus but of the immune reaction of the organism against viral antigens. Thus chronic inflammatory reaction observed in the liver of patients with CAH-B means that the organism is unable to eliminate the viral infection of the hepatocytes through the immune reaction. This pathogenic viewpoint on CAH-B and other forms of chronic viral hepatitis (C, D) stimulated us to stop treating patients with immune-suppressive and anti-inflammatory medication. After several years of attempting to treat patients with CAH-B with immuno-modulating compounds we came to the conclusion that the therapeutic use of the PADMA 28 herbal remedy is the most suitable means of achieving a clinical, biochemical, immunological and histological benefit. In the course of the past decade we have treated 126 adults and 52 children with CAH-B. Following a two-year treatment with PADMA 28 (daily dose: 3 x 2 tablets) the following results were achieved: About 90% of the patients had their biochemical parameters normalized and the number of the T-lymphocyte subsets (CD3, CD4, CD8, CD4/CD8) improved. In about 15% of patients viral infection was eliminated. About 70% of patients seroconverted from HBe-Ag positivity to anti-HBe. In around 10% of the patients no clinical or serological improvement was observed following the treatment. PADMA 28 was well tolerated by the patients. Their appetite and general wellbeing improved. Ultrasonographic tests of liver and spleen gave no indication of any cirrhotic lesions.

Keywords: PADMA 28; chronic active hepatitis; hepatitis B virus

Multiple sclerosis MS

Korwin-Piotrowska T, Nocon D, Stankowska-Chomicz A, Starkiewicz A, Wojcicki J, Samochowicz L

Experience of PADMA 28 in Multiple Sclerosis.

Phytotherapy Research 1992;6:133-6.

One hundred subjects suffering from a chronic progressive form of multiple sclerosis were randomly divided into two equal groups. Group 1 received PADMA 28, two tablets three times a day, and group 2, the control, was treated only symptomatically. Treatment and observation lasted for 1 year. Examinations performed directly prior to the study and in the course of observation included: neurological state, visual and auditory evoked potentials, basic laboratory tests. A positive effect of PADMA 28 was observed in 44% of patients with multiple sclerosis in the form of improvement of general condition, increase of muscle strength, decrease or disappearance of disorders affecting sphincters. In 41% of patients with initially an abnormal tracing of visual evoked potentials, an improvement or normalization was achieved. Of patients, who did not receive PADMA 28 none felt better, moreover, 40% of them showed a deterioration. Tolerance of the drug was excellent.

Keywords: multiple sclerosis; PADMA 28; treatment in 100 patients

Immune defence

Jankowski A, Jankowska R, Brzosko WJ

Treatment of children prone to infection with PADMA 28.

Schweiz Zschr für GanzheitsMedizin 1992;4(7/8 Suppl 1):22-3.

The 3 year study covered 305 children. Only those children were included who during the preceding 9 months had suffered at least one infection per month, including at least 3 times bronchitis and/or pneumonia. Three months before treatment with PADMA 28 medication with steroids was discontinued. The same applied to medication with antibiotics which was discontinued at least two weeks before medication with PADMA 28. The efficacy of the treatment was evaluated by the frequency and severity of respiratory infection during 9 months of treatment. 71.5 % of the patients showed a clear improvement in their condition.

Other studies have shown the following effects of PADMA 28 on the immune system of patients: it improves the phagocytic activities of macrophages versus bacteria and immune complexes. It can normalize the CD4/CD8 index of the T-lymphocytes. Furthermore, PADMA 28 can increase the synthesis of interferons, Interleukin-1, Interleukin-2 and the migration inhibition factor.

Keywords: PADMA 28; respiratory tract infections

Heart diseases

Zebrowski MR E

The role of regulatory systems in inflammatory heart disease

Erfahrungsheilkunde 2004;53:81-8.

Inflammatory heart diseases are one of the main causes of death in Western society. The immeasurable complexity of the cytokine and receptor network responsible for the regulation of the inflammatory reaction in the organism is the reason why until today no effective methods of therapeutic intervention in its individual elements have been developed. In the case of inflammatory heart disease the focus should be placed on how to increase the “organism’s regulatory capacity”, i.e. the regulatory system’s ability not to generate an inflammatory response to the given enhanced stimulus. The synergistic herbal treatment offers an opportunity for the regulatory system’s efficiency to recover. A herbal drug with these broad, multidirectional effects on the organism is PADMA 28, which owes its properties to a unique composition of active substances found in 20 medicinal herbs selected in accordance with a Tibetan formula.

Keywords: Regulatory systems, Padma 28, herbal multi-component drug, anti-inflammatory and immunomodulatory adjuvant therapy of heart diseases

Dental pulpitis

Füllemann F

Padma 28 in the treatment of chronic dental pulpitis: an observational case study in 49 patients

Forsch Komplementärmed 2006;13(Suppl 1):28–30.

In the case of pulpitis the dentist has to differentiate between a reversible and therefore treatable pulpal inflammation and an irreversible damage of the pulpa, according to the clinical symptoms. From these one cannot draw conclusions about the effective histological condition of the pulpa. Early stages of pulpitis cannot be recognized by X-ray either. Objectives: By means of case studies in the course of daily dental practice the following questions are addressed: Is dental pulpitis an indication for the use of the Tibetan remedy Padma 28? Can a root canal treatment be prevented by administering Padma 28? What dosage is appropriate in this indication? Patients and Methods: 53 patients with symptoms of chronic dental pulpitis but without clear indication for an immediate root canal treatment were prescribed 2 × 2 tablets Padma 28 daily, for 15 days. 49 patients took the preparation, and the course of symptoms was recorded and analyzed according to a simple scheme. Results: 27 of these patients (55%) were free of pain within 1 month. A total of 40 patients (81%) reached a pain-free state after a longer period. By now, in most cases observations have been made for a period of 2–3 years (maximum: 5,5 years). 12 patients (24%) remained without relapse so far for more than 3 years. These experiences allow to deduce possible indications and clinical symptoms for the use of Padma 28. Conclusions: These results encourage the use of Padma 28 as a complementary preparation with little side effects, in unclear cases of pulpitis. The clinical development can be observed without further treatment if the patient does not need pain medication. Most patients (>80%) showed a complete remission, positively affected and expedited by Padma 28; root canal treatments or extractions could be prevented. In many cases the improvement has sustained over observation periods of >3 years. Criteria for therapeutic decisions are proposed.

Keywords: Padma 28, pulpitis, tooth, inflammation, Tibetan medicine, root canal

Clinical experiences in the general practice

Bommeli C, Bohnsack R, Kolb C

Clinical experiences in the general practice with a multicomponent preparation derived from Tibetan medicine

Erfahrungsheilkunde 2001;50(11):745-56.

A total of 147 retrospective practical-experience reports from 15 Swiss doctors on treatment with the multi-substance preparation PADMA 28 were collected and evaluated. In an average of 60% of the cases the product was used successfully in the treatment of circulatory disorders in everyday general practice. Together with the treatment of cardiovascular diseases and cerebral circulatory disorders, arteriosclerotic diseases thus constitute the main field of application (75%). These indications include memory problems, tinnitus and visual disorders. In general practice, other chronic inflammatory conditions such as back ailments and joint pain, as well as dizziness, asthenia, weariness, respiratory disorders, phlebitis and allergies are further indications for the product (25%).

The efficacy was assessed largely as good (75%) by both the doctors and the patients. The good assessment of the tolerability (94% of the doctors and 85% of the patients) and the drug form (82%) is reflected in the good compliance (87%).

About one-quarter of all the patients were treated only with PADMA 28. The good results of the monotherapy with the Tibetan remedy of initial symptoms of peripheral circulatory disorders are of particular significance for the prevention and treatment of arteriosclerotic disease.

Keywords: atherosclerosis; chronic inflammation; case reports; Tibetan medicine; PADMA 28

Review

Überall F, Fuchs D

Chronic inflammation: Modulation of the cytokine network by PADMA 28.

Schweiz. Zschr. GanzheitsMedizin 2004 Oct,16(6):360-2.

[Article in German, Abstract in English available]

The Tibetan herbal remedy PADMA 28 revealed promising results in the supportive treatment of intermittent claudication, atherosclerosis and chronic hepatitis B. Previous studies confirmed its anti-oxidative and anti-inflammatory properties. The effect of PADMA 28 was investigated in stimulated and unstimulated human peripheral blood mononuclear cells (PBMC) in vitro, monitoring the metabolism of neopterin and tryptophan. Stimulation of PBMC with the mitogens phytohaemagglutinin and concanavalin A induced neopterin formation and tryptophan degradation ($p < 0,001$) compared to unstimulated PBMC. PADMA 28 inhibited both immunobiochemical reactions ($p < 0,001$) in a concentration-dependent manner, higher concentrations of PADMA 28 were able to completely block the pathways induced by mitogenic stimulation. Data allow to conclude that PADMA 28 is able to inhibit immunobiological effects in stimulated PBMC in vitro. The suppression of neopterin production and tryptophan degradation suggests a specific influence on Th1-induced immune reaction, especially on the cytokine interferon- γ . The relevance of these findings for depressive mood changes induced by chronic inflammation is discussed.

Keywords: Tibetan medicine; PADMA 28; depressive mood, Indoleamine (2,3)-dioxygenase, Neopterin, Tryptophan, chronic inflammation, cytokine

Schwabl H, Vennos C.

Chronic Inflammation and Extracellular Matrix ECM: Starting Point for an Anti-Inflammatory Intervention Scheme

Schweiz. Zschr. GanzheitsMedizin 2007,19(5):269-76

Background: In inflammation a signal cascade is set in motion, which sustains itself via positive feedback mechanisms. If in spite of the elimination of the underlying cause of the inflammation these feedback loops can not be interrupted, the inflammation becomes chronic. Chronic inflammations stop being a part of the normal healing process. As a discrete aspect of pathogenesis they often harm the body tissue more than the initial cause of inflammation. The complex inflammatory processes encompass more than the interaction of cellular protagonists and their cytokines. With the system of the ground regulation complementary medicine offers an expanded functional space, in which immune cells and mesenchymal cells interact with the extracellular matrix, the structured interstitium, as well as the capillary blood system, nerve endings and lymph vessels. **Objective and method:** The immunologic view of the inflammatory reaction is compared to the system of the ground regulation according to A. Pischinger and H. Heine. The question is analysed, whether from this comparison new integrative approaches result regarding an anti-inflammatory therapy as well as prevention and aftertreatment of chronic inflammatory diseases. **Results:** Not only different anti-inflammatory molecules are necessary for termination of inflammatory reactions, especially in chronic inflammations the regeneration of the regulatory capacity of the system of ground regulation is essential. Only triggering and amplifying anti-inflammatory impulses initiate the actual healing phase. From this concept a three-step intervention schema can be derived, which is focused on the extracellular matrix: through the three phases of therapy, "reload-protect-trigger", different functions of the extracellular matrix can be addressed. By means of examples this integrative concept is explained and transferred into a schema applicable in practice. This allows the easy assessment of the relevance of individual treatments to the three-step functional model of the extracellular matrix in everyday life. The integrative point of view seems necessary insofar as especially in the area of chronic inflammations a multitude of methods are applied but an overall therapy concept is often missing.

Keywords: extracellular matrix, ground regulation, chronic inflammation, herbal medicine, complementary medicine, CAM

Tibetan medicine in Europe

Schwabl H, Vennos C

The "multi-target" approach of Tibetan remedies - Mechanisms of action of Padma 28 in inflammation, with the example of atherosclerosis

Schweiz Zschr GanzheitsMedizin 2006;18(4):213-8.

Chronic inflammation poses high demands on modern medicine. Multifactorial chronic diseases require multilevel therapies that work on different pathogenic processes and at the same time have few side effects. Due to their multicomponent composition and their high tolerability Tibetan medicines offer valuable therapeutic approaches. Tibetan formulas are multicomponents containing different, mostly herbal raw material. Their composition is based on the principles of Tibetan medicine. Therapeutically cooling or warming formulas are used to counterbalance the disturbed equilibrium of bodily energies. Because of the complex pharmacological activity profile of Tibetan remedies they act as "multi-target drugs". The concept of multi-target drugs comprises partial effects at multiple sites of action simultaneously. Such a profile of activity is not limited to a strong effect at only one site of action as it occurs in the case of single-target drugs. This multi-target approach seems especially appropriate in multifactorial, chronic diseases.

The multicomponent formula Padma 28 is based on Tibetan medicine. In clinical, in-vitro und ex-vivo studies it showed promising effects on atherosclerotic changes. The comparison of these scientific results and the processes in atherogenesis clearly proves the character of Padma 28 as a multi-target drug. The multicomponent interacts with the pathogenic processes simultaneously at different sites of the artery wall and in different stages of the disease. The example of Padma 28 in atherosclerotic changes shows that Tibetan medicines act as multi-target drugs and offer promising therapeutic approaches, especially in chronic diseases with complex etiology. The subject of multi-target drugs represents an important contribution to the modern understanding of Tibetan medicines and complementary practice in general.

Keywords: Tibetan Medicine, atherosclerosis, multi-target drug, multicomponent, Padma 28

In vitro studies

Exner M, Raith M, Holzer G, Gmeiner B, Wagner O, Kapiotis S

Anti-inflammatory mechanisms of the Tibetan herbal preparation Padma 28 in the vessel wall

Forsch Komplementärmed 2006;13(Suppl 1):13–7.

The Tibetan herbal preparation Padma 28 has been shown to act as an anti-atherosclerotic agent in advanced peripheral arterial occlusive disease. We tested the effect of aqueous Padma 28 extracts on both the C-reactive protein (CRP) induced expression of the pro-inflammatory cell adhesion molecule E-selectin and the anti-atherosclerotic protective enzyme heme oxygenase-1 (HO-1) in human aortic endothelial cells. Methods and Results: According to FACS analysis, quantitative RT-PCR and Western blot, CRP-induced E-selectin expression was completely prevented by aqueous Padma 28 extracts. Additionally, Padma 28 mediated an up to 60-fold upregulation of HO-1 mRNA as measured by quantitative RT-PCR. This upregulation could also be demonstrated on the protein level. Conclusion: Aqueous extracts of the Tibetan herbal preparation Padma 28 inhibit CRP-induced expression of the inflammatory cell adhesion molecule E-selectin and lead to upregulation of the vascular protective enzyme HO-1 in human aortic endothelial cells. These properties may be responsible for its antiatherosclerotic effects in peripheral arterial occlusive disease.

Keywords: Padma 28, atherosclerosis, inflammation, C-reactive protein, E-Selectin, heme oxygenase-1

Barak V, Kalickman I, Halperin T, Birkenfeld S, Ginsburg I

PADMA 28, A Tibetan herbal preparation is an inhibitor of inflammatory cytokine production.

Eur Cytokine Netw 2004 Sept;15(3):203-9.

Background: Previous studies have shown that PADMA 28, a multicomponent, traditional Tibetan herbal plant preparation possesses a variety of beneficial effects on several experimental models of inflammatory and immune processes, including autoimmune diabetes and autoimmune encephalomyelitis. In humans, PADMA 28 attenuated the symptoms associated with intermittent claudications in atherosclerotic patients. Objective: To assess the effect of PADMA 28 on the immune system, e.g. cytokine (interleukins) production. Design: Cytokine production by human blood monocytes (derived from 12 healthy donors) stimulated in vitro, either by endotoxin (LPS) from *Salmonella typhi* or by lipoteichoic acid (LTA) from group A *Streptococci* was modulated by PADMA-28. Results: The present study showed that an aqueous extract of PADMA 28 strongly decreased the production of the inflammatory cytokines IL-1 β , IL-6, IL-8 and TNF- α , and more moderately, also decreased the anti-inflammatory cytokine IL-10 induced by LPS. However, the LTA – induced IL-10 production was [not significantly] increased by the low dose PADMA 28, while not effected at all by the higher dose of PADMA 28. Conclusions: The data from these finding suggest a possible clinical efficacy of PADMA 28 either in autoimmune and in inflammatory conditions or in post-inflammatory sequelae, as previously shown in vivo and human studies, probably by decreasing inflammatory cytokines.

Keywords: PADMA 28, herbal medicine, inflammatory cytokines