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Wissenschaftliche Studien zur Wirkungsweise von Tibetischen Arzneimitteln

Scientific Studies on the mode of action of Tibetan Medicines

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Publikationen zu Tibetischen Komplexformeln aus der Datenbank Pubmed (www.pubmed.com) mit Zusammenfassungen

Publications on Tibetan complex formulas from the Pubmed database (www.pubmed.com) with abstracts

Anmerkung: Dieser Index umfasst eine Auswahl von wissenschaftlichen Arbeiten zur Wirkungsweise von Tibetischen Arzneimitteln und darin verwendeten Pflanzen. Er ist ausschliesslich zur Information von Ärzten/Ärztinnen und Apothekern/Apothekerinnen gedacht.

Note: This index contains a selection of scientific studies on the mode of action of Tibetan medicines and is intended only as an information for doctors and pharmacists.

Neurogastroenterol Motil. 2010;22:1036-41.

Effects of the Tibetan herbal formula Padma Lax on visceral nociception and contractility of longitudinal smooth muscle in a rat model.

Gschossmann JM, Kraymer M, Flogerzi B, Balsiger BM.

BACKGROUND: The high prevalence of functional bowel disorders among the general population contrasts with the limited number of pharmacological treatment options for this condition. This has led to an interest for alternative therapeutic approaches. Padma Lax is an herbal laxative on the basis of Tibetan formulas. Our aim is to examine the effect of Padma Lax on visceral nociception in vivo and (B) on contractile activity of longitudinal smooth muscle of the lower gut in vitro and ex vivo. **METHODS:** (A) Visceral sensory function in response to colorectal distension was assessed by abdominal wall electromyography in male Wistar rats pretreated with Padma Lax. (B) Effects of Padma Lax on contractility of gut smooth muscles were studied both in vitro with superfusion of the agent and ex vivo following oral administration of the preparation. Activities were measured as area under the curve. **KEY RESULTS:** (A) For visceral sensitivity, no differences were observed between the Padma Lax and the control group. (B) Proximal colon muscle strips of the Padma Lax pretreated group showed significantly lower spontaneous contractility ex vivo than controls. Cholinergic procontractile stimulation was reduced in Padma Lax pretreated group and in colon strips of naive rats when Padma Lax was superfused in vitro (all $P < 0.05$). **CONCLUSION & INFERENCES:** Cholinergic mechanisms appear to be important in the modulation of rat proximal colon contractility of orally and directly applied Padma Lax. These findings help elucidate a potential mechanism of action of this herbal remedy which has undergone clinical testing in patients with constipation predominant irritable bowel syndrome.

Arch Dermatol Res. 2010;302:669-77.

A multi-component herbal preparation (PADMA 28) improves structure/function of corticosteroid-treated skin, leading to improved wound healing of subsequently induced abrasion wounds in rats.

Aslam MN, Warner RL, Bhagavathula N, Ginsburg I, Varani J.

PADMA 28 is a multi-component herbal mixture formulated according to an ancient Tibetan recipe. PADMA 28 is known to stimulate collagen production and reduced levels of collagen-degrading matrix metalloproteinases (MMPs). The goal of the present study was to determine whether topical treatment of rat skin with PADMA 28 would improve skin structure/function, and whether subsequently induced abrasion wounds would heal more rapidly in skin that had been pretreated with PADMA 28. Hairless rats were exposed to a potent topical corticosteroid (Temovate) in combination with either DMSO alone or with PADMA 28 given topically. At the end of the treatment period, superficial wounds were created in the skin, and time to wound closure was assessed. Collagen production and matrix-degrading MMPs were assessed. Abrasion wounds in skin that had been pretreated with PADMA 28 healed more rapidly than did wounds in Temovate plus DMSO-treated skin. Under conditions in which improved wound healing was observed, there was an increased collagen production and decreased MMP expression, but no significant epidermal hyperplasia and no evidence of skin irritation. The ability to stimulate collagen production and inhibit collagen-degrading enzymes in skin and facilitate more rapid wound closure without irritation should provide a rationale for development of the herbal preparation as a "skin-repair" agent.

Clin Exp Immunol. 2009;157:155-64.

Amelioration of hepatic fibrosis via Padma Hepaten is associated with altered natural killer T lymphocytes.

Ginsburg I, Koren E, Horani A, Mahamid M, Doron S, Muhanna N, Amer J, Safadi R.

Hepatic fibrosis is the end-stage consequence of chronic liver disease, affecting many people worldwide. Unlike the anti-fibrotic effect of natural killer (NK) cells, CD8 and NK T subsets are considered as profibrogenic subsets. Padma Hepaten is a multi-compound herbal preparation derived from Tibetan medicine and has proven efficacy in some clinical trials and tests at the cellular level. In this study, we evaluate the immune efficacy of Padma Hepaten administered intraperitoneally (i.p.) and/or orally in a mice model of hepatic fibrosis. Hepatic fibrosis was induced by 6 weeks of biweekly i.p. carbon tetrachloride (CCl₄) injections in male C57Bl6 mice. There were four groups, including naive mice, non-treated fibrotic mice and fibrotic mice treated by Padma Hepaten at weeks 5-6 of fibrosis induction either orally or by i.p. injections. Padma Hepaten was

prepared at 10 mg/ml in saline and 250 microl (2.5 mg) were administered four times per week. After week 6, animals were killed. To isolate a Padma Hepaten-associated effect on lymphocytes, splenocytes were harvested from either naive or Padma Hepaten-treated non-fibrotic donors. Isolated splenocytes were therefore reconstituted into two groups of irradiated recipients. Recipients were then administered the same CCl₄ regimen. Hepatic fibrosis was determined by sirius red staining of liver sections and by assessment of alpha smooth muscle actin expression compared with beta-actin (both by mRNA as well as the protein liver extract western blotting). Hepatic fibrosis and alanine aminotransferase serum levels were decreased significantly in both Padma Hepaten-treated groups compared with the non-treated fibrotic group. Padma Hepaten treatment was associated with attenuation of lymphocyte subsets in both treated groups. Using a chemiluminescence technique to assess total anti-oxidant capacities (TAC), it was found that both the plasmas and livers of mice treated by CCl₄ had significantly higher TAC compared with controls. However, the levels of TAC in animals treated either by CCl₄ alone or CCl₄ with Padma Hepaten were similar. Adoptive transfer of Padma Hepaten-treated lymphocytes was associated with fibrosis amelioration compared with recipients with naive lymphocytes. CCl₄ generates higher levels of anti-oxidant capacities, probably as a response to oxidative stress. Padma Hepaten administration attenuated hepatic fibrogenesis significantly, accompanied by attenuation of lymphocyte but not anti-oxidant capacities.

J Midwifery Womens Health. 2009;54:133-141.e1.

Randomized double masked trial of Zhi Byed 11, a Tibetan traditional medicine, versus misoprostol to prevent postpartum hemorrhage in Lhasa, Tibet.

Miller S, Tudor C, Thorsten V, Nyima, Kalyang, Sonam, Lhakpen, Droyoung, Quzong K, Dekyi T, Hartwell T, Wright LL, Varner MW.

The objective of this study was to compare a Tibetan traditional medicine (the uterotonic Zhi Byed 11 [ZB11]) to oral misoprostol for prophylaxis of postpartum hemorrhage (PPH). We conducted a double-blind randomized controlled trial at three hospitals in Lhasa, Tibet, People's Republic of China. Women (N = 967) were randomized to either ZB11 or misoprostol groups. Postpartum blood loss was measured in a calibrated blood collection drape. The primary combined outcome was incidence of PPH, defined as measured blood loss (MBL) > or = 500 mL, administration of open label uterotonics, or maternal death. We found that the rate of the combined outcome was lower among the misoprostol group (16.1% versus 21.8% for ZB11; P = .02). Frequency of PPH was lower with misoprostol (12.4% versus 17.4%; P = .02). There were no significant differences in MBL > 1000 mL or mean or median MBL. Fever was significantly more common in the misoprostol group (P = .03). The rate of combined outcome was significantly lower among women receiving misoprostol. However, other indices of obstetric hemorrhage were not significantly different.

BMC Complement Altern Med. 2008;8:51.

In vivo effects of Pain Relieving Plaster on closed soft tissue injury in rabbit ears.

Wang YZ, Guo CY, Zhong HG, Zhang WN, Wang DL, Wang X, Dong FH.

BACKGROUND: Soft tissue injury imposes major public health burdens worldwide. The positive effect of China's Tibetan medicine and the *Lamiophlomis rotata*-based herbal Pain Relieving Plaster (PRP) on healing closed soft tissue injury (CSTI) has been reported. The herbs contained in Plaster are also referred as 'blood-activating and stasis-dispelling' in herbal medicine. The formula of the plaster contains four China's Tibetan medical herbs, including *Lamiophlomis rotata*, *Oxytropis falcate* Bunge, *Curcuma longa* Linn, and *Myricaria bracteata*. Two of these herbs (*Lamiophlomis rotata*; *Curcuma longa* Linn) are commonly used in different formulae of Chinese medicine. The objective of this study is to use an interdisciplinary approach to test the hypothesis that the formula and its components influence the process of CSTI. **METHODS:** In vivo models have been established in 30 rabbit ear pinnae and studied for: (1) blood flow velocity (BFV) which was affected by pressure of 21.2 kg/cm² for 30 second over the local rabbit ear tissue; (2) edema formation of the closed soft tissue injury; (3) in vivo local temperature change. **RESULTS:** The results of in vivo studies indicated that CSTI significantly increased the velocity of blood flow and increased edema formation within the control group. The PRP extracts for 5 hours significantly slowed down the BFV of CSTI in rabbit ears, markedly decreased the elevated edema level from the 3rd to the 5th day. **CONCLUSION:** The ingredients contained in the formula have positive effects in healing CSTI and further study is worth exploring.

Artherosclerosis 2006,189:39-46.

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

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

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.

Zhongguo Zhong Xi Yi Jie He Za Zhi. 2006;26:202-4.

[Clinical study on effect of fluoxetine combined with Chinese medicine or tibetan drugs in treating senile depression in plateau district] Article in Chinese

Zhang HW, Wang CY, Xu HN, Zhao X, Dai Q, Li J, Du X, Song Z, Han G, Liu G, Li P, Lin H.

OBJECTIVE: To compare the effect and side-effect of fluoxetine and combination of fluoxetine and Chinese or Tibetan medicine in treating senile depression in plateau district. **Methods** Ninety patients with diagnosis of senile depression conformed to CCMD-3 standard, in plateau district of 2260 - 3200 m altitude were randomly divided into three groups and treated with fluoxetine (group A), fluoxetine plus Sanpu Xinnao Xin granule (group B) and fluoxetine plus Xiaoyao pill (group C), respectively, 30 cases in each group. Therapeutic effects were evaluated with Hamilton's depressive scale (HAMD) and treatment emergent symptom scale (TESS) after 6 weeks treatment. **RESULTS:** There was no significant difference in the therapeutic effects between the three groups. The adverse reaction in Group B and C was less than that in Group A ($P<0.01$). **Conclusion** Sanpu Xinnao Xin granule and Xiaoyao pill can raise the tolerance of patients with senile depression in plateau area against the adverse reaction of fluoxetine.

Forsch Komplementarmed. 2006;13 Suppl 1:31-2.

[Treatment of a tetraplegic patient with chronic constipation with the Tibetan remedy Padma Lax--a case report] Article in German

Feldhaus S.

BACKGROUND: In spinal cord injuries disturbed defecation, constipation and their concomitant disorders are frequent clinical symptoms. They may severely impair the quality of life of the affected patients. The presented case study and two more case reports, summarized in table form, outline therapeutic difficulties and therapy options in the treatment of constipation in paraplegic patients. **CASE REPORT:** A 69-year-old male patient with tetraplegia below C4 suffered from disturbed defecation, constipation with recurrent co-prostasis and pronounced meteorism which impeded breathing. Padma Lax was applied for several months, and constipation and the concomitant meteorism were noticeably reduced. **CONCLUSION:** The herbal preparation based on a formula from Tibetan Medicine may offer new therapeutic options in the care and treatment of patients with severe constipation. This report could also give first indications for controlled clinical studies in tetraplegic patients.

Padma 28 in der Behandlung von chronischen Zahnpulpitiden: Eine Praxisbeobachtung an 49 Fällen
[Padma 28 in the treatment of chronic dental pulpitis: an observational case study in 49 patients] Article in German

Füllemann F.

HINTERGRUND: Im Falle einer Pulpitis muss der behandelnde Zahnarzt die Differentialdiagnose zwischen einer reversiblen, also behandelbaren pulpalen Entzündung und einer irreversiblen Schädigung der Pulpa aufgrund der Symptome stellen. Rückschlüsse auf den tatsächlichen histologischen Zustand der Pulpa lassen sich aus den klinischen Symptomen nicht ziehen. Auch röntgenologisch kann ein frühes Pulpitisstadium nicht erkannt werden. **FRAGESTELLUNG:** Im Rahmen der zahnärztlichen Praxistätigkeit soll anhand von Fallauswertungen folgenden Fragen nachgegangen werden: Stellt Zahnpulpititis eine Indikation für den Einsatz des Tibetischen Arzneimittels Padma 28 dar? Kann durch Anwendung von Padma 28 eine Wurzelbehandlung vermieden werden? Welche Dosierung ist bei dieser Indikation zu empfehlen? **PATIENTEN UND METHODEN:** 53 Patienten mit chronischen Pulpitissymptomen, bei denen keine eindeutige Indikation für eine sofortige Wurzelbehandlung bestand, wurde Padma 28 2 × 2 Tabletten/Tag für 15 Tage verschrieben. 49 Patienten nahmen das Präparat ein. Der Verlauf der Beschwerden wurde anhand eines einfachen Schemas bewertet. **ERGEBNISSE:** 27 Patienten (55%) waren innerhalb eines Monats schmerzfrei, insgesamt wurden 40 Patienten (81%) innerhalb eines längeren Behandlungszeitraums schmerzfrei. In den meisten Fällen liegt der Beobachtungszeitraum zwischenzeitlich bei 2–3 Jahren (Maximum: 5,5 Jahre). 12 Patienten (24%) sind bereits seit über 3 Jahren beschwerdefrei. Aus diesen Erfahrungen lassen sich mögliche Indikationen und Beschwerdebilder für den Einsatz von Padma 28 ableiten. **SCHLUSSFOLGERUNGEN:** Padma 28 kann als nebenwirkungsarmes, naturheilkundliches Präparat bei Grenzfällen einer Pulpitis eingesetzt werden. Falls der Patient nicht zu Schmerzmitteln greifen muss, kann so die weitere Entwicklung der Beschwerden abgewartet werden. Bei der Mehrzahl der Patienten (>80%) zeigte sich eine Abheilung, die durch Padma 28 positiv beeinflusst oder beschleunigt wurde; eine Wurzelbehandlung oder Extraktion konnte vermieden werden. In vielen dieser Fälle ist die Besserung nachhaltig. Kriterien für die Therapieentscheidung werden vorgestellt.

BACKGROUND: 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 x 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.

Wirksamkeit und Sicherheit von Padma 28 bei peripherer arterieller Verschlusskrankheit
[Efficacy and safety of Padma 28 in peripheral arterial occlusive disease] Article in German

Melzer J, Brignoli R, Saller R.

HINTERGRUND: Das komplexe pflanzliche Arzneimittel Padma 28 basiert auf einer Formel der Tibetischen Medizin und wird seit über 30 Jahren in der Schweiz zur Behandlung von Durchblutungsstörungen und Symptomen der Claudicatio intermittens (reduzierte Gehstrecke) eingesetzt. **FRAGESTELLUNG:** Welche Evidenz liegt zur klinischen Wirksamkeit und Sicherheit dieses Arzneimittels bei Patienten mit peripherer arterieller Verschlusskrankheit (PAVK) vor? **MATERIAL UND METHODE:** Systematischer Review mit

Literaturrecherche in elektronischen Datenbanken (jeweils von deren Beginn bis Herbst 2005) und den Literaturverzeichnissen der gefundenen Arbeiten. **ERGEBNISSE:** Es fanden sich 14 Artikel (6 publizierte, 1 unpublizierte und 6 doppelt publizierte Studien sowie 1 Metaanalyse). Sechs Studien untersuchten die maximale Gehstrecke, fünf davon zeigten eine signifikante Zunahme derselben. Die gepoolten Daten der Metaanalyse bestätigten eine signifikante und klinisch relevante Verlängerung der Gehstrecke um mehr als 100 m bei knapp einem Fünftel der Patienten. Die schwerwiegenden unerwünschten Ereignisse standen nicht im Zusammenhang mit dem Verum, die nicht schwerwiegenden waren gleich häufig wie unter Placebo. **SCHLUSSFOLGERUNGEN:** Die verfügbare Evidenz zeigt, dass die Multi-Target-Therapie mit Padma 28 eine statistisch signifikante und klinisch relevante Besserung von Symptomen der PAVK, d.h. eine erhöhte Gehstrecke, bewirkt.

BACKGROUND: The multicomponent herbal drug Padma 28 is based on a formula from Tibetan Medicine and has been used in Switzerland for over 30 years in the symptomatic treatment of circulatory disorders including intermittent claudication. **OBJECTIVE:** What is the current evidence regarding the clinical efficacy and safety of this drug in patients with peripheral arterial occlusive disease(PAOD)? **MATERIALS AND METHODS:** Electronic databases were searched (each from inception to fall 2005) as well as the reference lists of the relevant articles. **RESULTS:** 14 articles were found including 6 published studies, 1 un-published study, 6 double publications and 1 meta-analysis. Six studies analyzed maximum walking distance, 5 of these showed a significant increase. The pooled data of the meta-analysis confirmed a significant and clinically relevant increase of the maximum walking distance by more than 100 m in about 1 out of 5 patients. Serious adverse events were not related to verum, non-serious adverse events were equally frequent as under placebo. **CONCLUSIONS:** The evidence available shows that the multi-target therapy with Padma 28 provides statistically significant and clinically relevant relief from PAOD-related symptoms, i.e. an increased walking distance.

Forsch Komplementarmed. 2006;13 Suppl 1:18-22.

Antiproliferative properties of Padma Lax and its components ginger and elecampane.

[Antiproliferative Eigenschaften von Padma Lax und seinen Komponenten Ingwer und Alant] Artikel auf Englisch

Hofbauer S, Kainz V, Golser L, Klappacher M, Kiesslich T, Heidegger W, Krammer B, Hermann A, Weiger TM.

BACKGROUND: Padma Lax (PL) is a multi-component herbal laxative, derived from traditional Tibetan medicine. It has been used in the treatment of constipation dominant irritable bowel syndrome. Beyond its purgative and bowel-regulating properties we found it to exhibit antiproliferative properties. **MATERIALS AND METHODS:** C6 tumor cells were incubated with either an ethanolic or aqueous extract of PL. Cell proliferation, cell cycle, percentage of apoptotic cells, caspase-3/-7 activity as well as mitochondrial membrane potential were determined. **RESULTS:** Ethanolic extracts of PL inhibited cell proliferation in a dose- and time-dependent manner (half max concentration: 384.4 µg/ml after 48 h of incubation). Aqueous extracts were less effective. Ginger and elecampane were the active components of PL in respect to its antiproliferative action and were found to act synergistically. Supplementing the culture medium with polyamines could not override the cytostatic action of PL. Incubation of C6 cells with PL in the presence of catalase proved that the PL effect was specific and not due to oxidative stress. PL had no effects on the cell cycle at a low dose but arrested cells in G1 at high concentrations. Reduction of cell numbers was found to be due to apoptosis. The caspase-3/-7 pathway was not involved in the PL-induced cell death. However, mitochondrial membrane potential was lost during the course of incubation with PL indicating a mitochondrial- but not caspase-mediated induction of apoptosis. **CONCLUSION:** PL exhibits antiproliferative properties which may be beneficial to prevent constipation-related cancer. This study may also contribute to a future development of a new herbal-based antiproliferative treatment.

HINTERGRUND: Padma Lax (PL) ist ein auf einer Tibetischen Formel basierendes pflanzliches Laxativum, das bei der Behandlung des obstipationsdominanten Reizdarmsyndroms eingesetzt wird. In der vorliegenden Studie zeigen wir, dass PL auch eine antiproliferative Wirkung auf C6 Glioma-Zellen der Ratte hat. **MATERIAL UND METHODEN:** C6 Glioma-Zellen wurden mit ethanolischem oder wässrigem Extrakt von PL inkubiert. Die Zellproliferation, der Zellzyklus, der Prozentsatz apoptotischer Zellen, die Caspase-3/7-Aktivität sowie das Membranpotential der Mitochondrien wurden gemessen. **ERGEBNISSE:** Ethanolsche Extrakte von PL hemmen die Zellvermehrung in einer konzentrations- und zeitabhängigen Weise (halbmaximale Dosis 384.4 µg/ml nach 48 h Inkubation). Wässrige Extrakte waren weniger wirksam. Die Ingwerwurzel und die Alantwurzel konnten als die für die antiproliferative Wirkung verantwortlichen Komponenten in PL identifiziert werden. Durch Experimente unter Beigabe von Katalase konnte ausgeschlossen werden, dass die antiproliferative Wirkung nur auf einer oxidativen Stressreaktion beruht. PL hatte in niederen Dosierungen keine Wirkung auf den Zellzyklus, in hohen Konzentrationen wurde jedoch ein Arrest in G1 bewirkt. Eine Zugabe von Polyaminen konnte den

antiproliferativen Effekt von PL nicht aufheben. Die Reduktion der Zellzahl ist vor allem auf einen Apoptose-ähnlichen Zelltod zurückzuführen. Der Caspase-3/7-Signalweg war bei dem von PL induzierten Zelltod nicht involviert. Der durch Inkubation mit PL induzierte Verlust des mitochondrialen Membranpotentials deutete jedoch darauf hin, dass die Apoptose über den mitochondrialen Weg vermittelt wird. **SCHLUSSFOLGERUNGEN:** PL zeigt antiproliferative Eigenschaften, die die Vorbeugung obstipationsbedingter Tumore unterstützen könnte. Die vorliegenden Ergebnisse könnten auch prospektiv zur Entwicklung neuer antiproliferativer Agenzien auf naturstofflicher Basis beitragen.

Forsch Komplementarmed. 2006;13 Suppl 1:13-7.

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

[Antientzündliche Mechanismen des Tibetischen Pflanzenpräparats Padma 28 in der Gefäßwand] Artikel auf Englisch

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

BACKGROUND: 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 anti-atherosclerotic effects in peripheral arterial occlusive disease.

HINTERGRUND: Die tibetische Kräuterformel Padma 28 ist als wirksames Therapeutikum bei fortgeschrittener peripherer arterieller Verschlusskrankheit beschrieben worden. Wir untersuchten den Einfluss wässriger Padma-28-Extrakte auf die durch C-reaktives Protein (CRP) ausgelöste Expression des entzündungsassoziierten Zelladhäsionsmoleküls E-Selektin und des antiatherosklerotischen Schutzzyms Hämoxxygenase-1 (HO-1) in humanen aortalen Endothelzellen. **METHODEN UND ERGEBNISSE:** In FACS-Versuchen verhinderten wässrige Padma-28-Extrakte die CRP-induzierte Expression von E-Selektin an der Zelloberfläche. Dieser Effekt konnte auch in quantitativen RT-PCR-Versuchen auf mRNA-Ebene und im Western Blot gezeigt werden. Zusätzlich induzierte Padma 28 eine bis zu 60-fache Hochregulierung der HO-1 mRNA, ein Ergebnis, das auch auf der Proteinebene im Western Blot bestätigt werden konnte. **Schlussfolgerungen:** Wässrige Extrakte von Padma 28 führen zur Inhibition der CRP-induzierten E-Selektin-Expression und zur Hochregulierung des Schutzzyms HO-1 in Endothelzellen. Diese Eigenschaften könnten zur antiatherosklerotischen Wirkung von Padma 28 bei peripherer arterieller Verschlusskrankheit beitragen.

Forsch Komplementarmed. 2006;13 Suppl 1:7-12.

Das anti-inflammatorische Potential von Padma 28 – Übersicht experimenteller Daten zur antiatherogenen Wirkung und Diskussion des Vielstoffkonzepts

[Anti-inflammatory potential of Padma 28--review of experimental data on the antiatherogenic activity and discussion of the multi-component principle] Article in German

Ueberall F, Fuchs D, Vennos C.

HINTERGRUND: Das Tibetische Arzneimittel Padma 28 wird seit Jahrzehnten in Europa angewendet und hat sich besonders bei entzündlich und arteriosklerotisch bedingten Beschwerden als wirksam erwiesen. Neben klinischen Studien liegt eine grosse Anzahl von In-vitro- und Ex-vivo-Studien vor, die verschiedene Eigenschaften und biochemische Aktivitäten dieses komplex zusammengesetzten Pflanzenpräparates belegen. **Fragestellung:** Ziel ist es, anhand der vorliegenden Daten einen Überblick über das komplexe Wirkprofil von Padma 28 zu geben, die vorliegenden Erkenntnisse in Beziehung zur Entwicklung von Arteriosklerose zu setzen und anhand dessen das antiatherogene Potential von Padma 28 zu diskutieren. **METHODEN:** Die publizierten wissenschaftlichen, nichtklinischen Originalarbeiten über Padma 28 wurden erfasst und gemäss den darin untersuchten Wirkmechanismen klassifiziert. Die Resultate werden in Beziehung zu den kurz dargestellten Vorgängen der Atherogenese gesetzt, wobei verschiedene Wirkmechanismen herausgearbeitet und besonderes Gewicht auf neuere Arbeiten gelegt wurde. **ERGEBNISSE:** Das vielschichtige Wirkprofil von

Padma 28 umfasst vor allem direkte und indirekte anti-inflammatorische Wirkungen sowie weitere Kategorien von biochemischen Mechanismen. Diese lassen sich den komplexen Vorgängen der Atherogenese zuordnen. **SCHLUSSFOLGERUNGEN:** Die beschriebenen Mechanismen stützen das therapeutische Anwendungsgebiet von Padma 28 – periphere Durchblutungsstörungen sowie Erkrankungen des chronisch entzündlichen Formenkreises. Auch lässt die Vielzahl der Wirkmechanismen sowie der Wirkorte einen ersten Schluss auf die konzeptionelle Formulierung dieses Vielstoffgemischs zu.

BACKGROUND: The Tibetan remedy Padma 28 has been used in Europe for decades and has proved to be effective in inflammatory and atherosclerotic conditions. Beyond clinical trials, a large number of in vitro and ex vivo studies report various properties and biochemical activities of this complex herbal multicomponent. **OBJECTIVE:** To give an overview of the complex efficacy profile of Padma 28, to review available data, to relate findings to the development of atherosclerosis and thus to discuss the antiatherogenic potential of Padma 28. **METHODS:** Published non-clinical original papers on Padma 28 were collected and classified according to the studied mechanisms of action. Results were correlated to the briefly described sequences of atherogenesis and various mechanisms of action were elaborated, laying particular emphasis on more recent articles. **RESULTS:** The complex activity profile of Padma 28 spans mainly direct and indirect anti-inflammatory properties as well as further categories of biochemical actions. These can be related to the complex processes of atherogenesis. **CONCLUSIONS:** The described mechanisms support the therapeutic field of application of Padma 28, i.e. peripheral circulatory disorders as well as chronic inflammatory disorders. Moreover, the numerous effects as well as the diversity of sites of action allow to draw first conclusions on the conceptual design of this multicomponent formula.

Cochrane Database Syst Rev. 2006 Jan 25(1):CD004116.

Herbal medicines for treatment of irritable bowel syndrome.

Liu JP, Yang M, Liu YX, Wei ML, Grimsgaard S.

BACKGROUND: Traditional herbal therapies have been used for a long time to treat gastrointestinal disorders including irritable bowel syndrome, and their effectiveness from clinical research evidence needs to be systematically reviewed. **OBJECTIVES:** To assess the effectiveness and safety of herbal medicines in patients with irritable bowel syndrome. **SEARCH STRATEGY:** We searched the following electronic databases till July 2004: The Cochrane Library (CENTRAL), MEDLINE, EMBASE, AMED, LILACS, the Chinese Biomedical Database, combined with hand searches of Chinese journals and conference proceedings till end of 2003. No language restriction was used. **SELECTION CRITERIA:** Randomised controlled trials of herbal medicines compared with no treatment, placebo, pharmacological interventions were included. **DATA COLLECTION AND ANALYSIS:** Data were extracted independently by two authors. The methodological quality of trials was evaluated using the components of randomisation, allocation concealment, double blinding, and inclusion of randomised participants. **MAIN RESULTS:** Seventy-five randomised trials, involving 7957 participants with irritable bowel syndrome, met the inclusion criteria. The methodological quality of three double-blind, placebo-controlled trials was high, but the quality of remaining trials was generally low. Seventy-one different herbal medicines were tested in the included trials, in which herbal medicines were compared with placebo or conventional pharmacologic therapy. Herbal medicines were also combined with conventional therapy and compared to conventional therapy alone. Compared with placebo, a Standard Chinese herbal formula, individualised Chinese herbal medicine, STW 5 and STW 5-II, Tibetan herbal medicine Padma Lax, traditional Chinese formula Tongxie Yaofang, and Ayurvedic preparation showed significantly improvement of global symptoms. Compared with conventional therapy in 65 trials testing 51 different herbal medicines, 22 herbal medicines demonstrated a statistically significant benefit for symptom improvement, and 29 herbal medicines were not significantly different than conventional therapy. In nine trials that evaluated herbal medicine combined with conventional therapy, six tested herbal preparations showed additional benefit from the combination therapy compared with conventional monotherapy. No serious adverse events from the herbal medicines were reported. **AUTHORS' CONCLUSIONS:** Some herbal medicines may improve the symptoms of irritable bowel syndrome. However, positive findings from less rigorous trials should be interpreted with caution due to inadequate methodology, small sample sizes, and lack of confirming data. Some herbal medicines deserve further examination in high-quality trials.

J Carcinog. 2005;4:15.

Apoptosis induced by the Tibetan herbal remedy PADMA 28 in the T cell-derived lymphocytic leukaemia cell line CEM-C7H2.

Jenny M, Schwaiger W, Bernhard D, Wrulich OA, Cosaceanu D, Fuchs D, Ueberall F.

The Tibetan herbal remedy PADMA 28 revealed promising results to support treatment of atherosclerosis, Charot syndrome (intermittent claudication), chronic active hepatitis and infection of the respiratory tract. The remedy was confirmed to be closely linked with anti- and pro-oxidative properties in vitro. In this study, apoptogenic and survival effects of PADMA 28 were investigated in the T cell-derived lymphocytic leukaemia cell line CEM-C7H2. PADMA 28 led to a concentration-dependent inhibition of cell proliferation accompanied by the accumulation of CEM-C7H2 cells in subG1 phase, fragmentation of poly (ADP-ribose) polymerase (PARP) and nuclear body formation. Treatment with PADMA 28 rescued to some extent cells over-expressing Bcl-2 from apoptosis. This finding suggests that the mechanism of action of PADMA 28 may be via interference with Bcl-2 triggered survival pathways.

Atherosclerosis. 2005;181:1-7.

Complementary therapies for peripheral arterial disease: systematic review.

Pittler MH, Ernst E.

While peripheral arterial disease (PAD) affects a considerable proportion of patients in the primary care setting, there is a high level of use of complementary treatment options. The aim was to assess the effectiveness of any type of complementary therapy for peripheral arterial disease. A systematic review was performed. Literature searches were conducted on Medline, Embase, Amed, and the Cochrane Library until December 2004. Hand-searches of medical journals and bibliographies were conducted. There were no restrictions regarding the language of publication. The screening of studies, selection, data extraction, the assessment of methodologic quality and validation were performed independently by the two reviewers. Data from randomized controlled trials, and systematic reviews and meta-analyses, which based their findings on the results of randomized controlled trials were included. Seven systematic reviews and meta-analyses and three additional randomized controlled trials met the inclusion criteria and were reviewed. The evidence relates to acupuncture, biofeedback, chelation therapy, CO(2)-applications and the dietary supplements Allium sativum (garlic), Ginkgo biloba (ginkgo), omega-3 fatty acids, padma 28 and Vitamin E. Most studies included only patients with peripheral arterial disease in Fontaine stage II (intermittent claudication). The reviewed RCTs, systematic reviews and meta-analyses which based their findings on the results of RCTs suggest that G. biloba is effective compared with placebo for patients with intermittent claudication. Evidence also suggests that padma 28 is effective for intermittent claudication, although more data are required to confirm these findings. For all other complementary treatment options there is no evidence beyond reasonable doubt to suggest effectiveness for patients with peripheral arterial disease.

J. Invest. Dermatol. 2005;124:524-9.

PADMA 28: a multi-component herbal preparation with retinoid-like dermal activity but without epidermal effects.

Aslam MN, Fligiel H, Lateef H, Fisher GJ, Ginsburg I, Varani J.

PADMA 28, a multi-component herbal mixture formulated according to an ancient Tibetan recipe, was assessed for effects on human dermal fibroblasts and epidermal keratinocytes in monolayer culture, and for effects on human skin in organ culture. PADMA 28 stimulated survival of fibroblasts in monolayer culture. In fibroblast monolayer culture and human skin organ culture, levels of matrix metalloproteinase-1 (MMP-1; interstitial collagenase) were reduced and type I procollagen production was increased. When keratinocytes were examined, there was no evidence of growth stimulation over a wide range of PADMA 28 concentrations. At high concentration, PADMA 28 inhibited keratinocyte proliferation. When organ cultures of human skin were treated with PADMA 28, there was no evidence of hyperplastic growth in the epidermis. Topical treatment of rhino mice with PADMA 28 failed to induce epidermal hyperplasia and was completely non-irritating. The ability to stimulate collagen production and inhibit the major collagen-degrading enzyme in skin without inducing a hyperplastic response in the epidermis may provide a basis for development of the herbal preparation as a "skin-repair" agent.

VASA. 2005;34:11-7.

Effects of the Tibetan herbal preparation PADMA 28 on blood lipids and lipid oxidisability in subjects with mild hypercholesterolaemia.

Brunner-La Rocca HP, Schindler R, Schlumpf M, Saller R, Suter M.

BACKGROUND: Previous studies showed an anti-atherosclerotic effect of PADMA 28, an herbal formula based on Tibetan medicine. As the mechanisms of action are not fully understood, we investigated whether PADMA 28 may lower blood lipids and lipid oxidisability, and affect early endothelial dysfunction. **PATIENTS AND METHODS:** Sixty otherwise healthy subjects with total cholesterol $>$ or $=$ 5.2 mmol/l and $<$ 8.0 mmol/l were randomly assigned to placebo or PADMA 28, 3 x 2 capsules daily, for 4 weeks (double-blind). Blood lipids (total, LDL-, and HDL-cholesterol, triglycerides, Apo-lipoprotein A1 and B) and ex vivo lipid oxidisability were measured before and after treatment. In a subset of 24 subjects, endothelial function was assessed using venous occlusion plethysmography with intraarterial infusion of acetylcholine. Isolated LDL and plasma both untreated and pre-treated with PADMA 28 extract were oxidised by the radical generator AAPH. Conjugated diene formation was measured at 245 nm. **RESULTS:** Blood lipids did not change during the study in both groups. In contrast to previous reports in mild hypercholesterolaemia, no endothelial dysfunction was seen and, consequently, was not influenced by therapy. Ex vivo blood lipid oxidisability was significantly reduced with PADMA 28 (area undercurve: 5.29 \pm 1.62 to 4.99 \pm 1.46, $p = 0.01$), and remained unchanged in the placebo group (5.33 \pm 1.88 to 5.18 \pm 1.78, $p > 0.1$). This effect persisted one week after cessation of medication. In vitro experiments confirmed the prevention of lipid peroxidation in the presence of PADMA 28 extracts. Persistent protection was also seen for LDL isolated from PADMA 28-pretreated blood after being subjected to rigorous purification. **CONCLUSIONS:** This study suggests that the inhibition of blood lipid oxidisability by PADMA 28 may play a role in its anti-atherosclerotic effect.

Antibiot Khimioter. 2005;50:23-6.

[Hepatoprotective effect of Tibetan remedy "Dig-Da-Shi-Tan"]. Article in Russian

Nikolaev SM, Sambueva ZG, Aseeva TA, Chekhirova GV.

In experiments on albino rats with toxic hepatitis due to their exposure to tetracycline hydrochloride it was shown that a course of therapeutic and preventive administration of Dig-da-shi-tan decoction had a strong hepatoprotective effect. Antioxidative, membrane integrative, cholagogic and antiinflammatory activities of the remedy were revealed.

Patol Fiziol Eksp Ter. 2005;(1):23-5.

[Mechanisms of immunotropic effect of the drug composition Taban-Arshan (Tibet medicine) on lymphocytes of patients with early rheumatoid arthritis and atopic bronchial asthma] Article in Russian

Semenova Llu, Salmasi ZhM, Kazimirskii AN, Poriadin GV.

The extract of the Tibetan medicine Taban-Arshan corrects changes of the immune system in inflammatory diseases--rheumatoid arthritis and atopic bronchial asthma. An immunomodulating effect of the drug consists in its ability to suppress hyperactivation of lymphocytes by normalization of expression of basic activation antigens.

Bull Exp Biol Med. 2004;138:65-6.

Taban-Arshan: immunocorrector in atopic bronchial asthma.

Semenova LY, Salmasi ZhM, Kazimirskii AN, Poryadin GV.

Taban-Arshan extract decreased expression of T-lymphocyte activation markers, normalized T-cell-mediated immunity, and suppressed increased activity of natural killer receptors during culturing with lymphocytes of patients with atopic bronchial asthma. Taban-Arshan extract normalized activation processes in the B-cell immunity and stimulated expression of receptors of activation-induced apoptosis.

Eur. Cytokine Netw. 2004;15:203-9.

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

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

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 in vivo and human studies, probably by decreasing inflammatory cytokines.

Int. Immunopharmacol. 2004;4:833-9.

PADMA 28 modulates interferon-gamma-induced tryptophan degradation and neopterin production in human PBMC in vitro.

Neurauter G, Wirleitner B, Schroecksnadel K, Schennach H, Ueberall F, Fuchs D.

Tibetan herbal remedy PADMA 28 revealed promising results to support treatment of intermittent claudication, atherosclerosis and chronic hepatitis. The remedy was confirmed to be closely linked with anti- and pro-oxidative properties in vitro. In this study, effect of PADMA 28 was investigated in stimulated and unstimulated human peripheral blood mononuclear cells (PBMC) in vitro. Neopterin production and tryptophan degradation were measured in supernatants of PBMC in the presence or absence of mitogens phytohaemagglutinin (PHA) and concanavalin A (Con A). Stimulation of PBMC induced neopterin formation and tryptophan degradation ($p < 0.001$ compared to unstimulated PBMC), and PADMA 28 inhibited both immunobiochemical effects ($p < 0.001$) in a concentration-dependent manner. Higher concentrations of PADMA 28 were more effective and were able to completely block the pathways induced upon 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 biochemical pathways induced by Th1-type cytokine interferon-gamma. Copyright 2004 Elsevier B.V.

Inflammopharmacology. 2004;12:373-89.

PADMA-28, a traditional Tibetan herbal preparation, blocks cellular responses to bFGF and IGF-I.

Navab R, Aingorn H, Fallavollita L, Sallon S, Mechoulam R, Ginsburg I, Vlodaysky I, Brodt P.

The growth factors basic fibroblast growth factor (bFGF) and insulin-like growth factor 1 (IGF-I) have been implicated in the pathophysiology of atherosclerosis and restenosis. The Tibetan herbal preparation PADMA-28 (a mixture of 22 plants which is used as an anti-atherosclerosis agent) was tested for its ability to inhibit the mitogenic activity of bFGF and IGF-I, growth factors involved in restenosis, atherosclerosis and tumour progression. DNA synthesis and proliferation of vascular smooth muscle cells, in response to serum bFGF, thrombin, or combinations thereof, were abrogated in the presence of microgram amounts of both the aqueous and organic, partially purified, extracts of PADMA-28. These fractions also inhibited IGF-I-mediated proliferation, migration and invasion of tumour cells responsive to IGF-I. The inhibition by PADMA 28 was reversible upon removal of the PADMA extracts, indicating that the effects were not related to cell toxicity. These and other properties (i.e., anti-oxidant activity) of PADMA-28 may be responsible for its beneficial effect as an anti-atherosclerotic agent, suggesting that this herbal preparation may have potential applications in the prevention of intimal hyperplasia and arterial stenosis secondary to coronary angioplasty and bypass surgery, as well as in the prevention and treatment of other vascular diseases and tumour growth and metastasis.

Inflammopharmacology. 2004;12:305-20.

Novel chemiluminescence-inducing cocktails, part II: measurement of the anti-oxidant capacity of vitamins, thiols, body fluids, alcoholic beverages and edible oils.

Ginsburg I, Sadovnic M, Oron M, Kohen R.

Using two luminescence-inducing cocktails, two distinct patterns of inhibition of light by different anti-oxidants have been identified, comprising Group A, in which a complete inhibition of light emission which is then followed by re-emergence of light, forming apparent S-shaped curves or similar shapes. This light pattern is induced by the "classical" anti-oxidants, ascorbate, vitamin E, uric acid, thiols, deferoxamine, as well as by anti-oxidant agents present in plasma, saliva, urine and in extracts derived from black coffee, and Group B, in which a gradually emerging "mound"-shaped pattern of light was seen with extracts from the Tibetan plant mixture PADMA-28, elderberry (Sambucol), grape seeds, green and black teas, apple, parsimony, red wines, edible oils and SOD. While the results with the Group A agents point to the presence of probably a single, major, anti-oxidants relatively sensitive to oxidation, Group B agents probably include a mixture of anti-oxidants which are more resistant to oxidation. It was also shown that agents from Group B could protect agents from Group A against consumption by the oxidants generated by the cocktails. It is proposed that these simple to use cocktails which probably generate a multiplicity of oxidants mimicking those generated by activated phagocytes, can rapidly assess the total anti-oxidant capacities (TAOC) in body fluids derived from patients suffering of excessive oxidative stress. Also, this technique may be useful in determining the content of dietary anti-oxidants recommended as supplements to enhance the resistance against excessive oxidation of lipids.

Antibiot. Khimioter. 2003;48:24-6.

[Effect of hepatophyt on the choleric function of the liver damaged by tetracycline] Article in Russian

Nikolaev SM, Sambueva ZG, Chekhirova GV, Tsyrenzhalov AV.

In experimental injury of the liver in Wistar-line white rats induced by tetracycline the course therapeutic and prophylactic administration of the dry extract "Hepatophyt" in a dose of 0.1 g/kg inhibits the negative effect of tetracycline and promotes stimulation of choleric and antitoxic functions of the liver. The dry extract was derived from the herbal mix of the same name, used in the practice of Tibetan medicine against liver diseases.

Forsch Komplementarmed Klass Naturheilkd. 2002;9:346-51.

Comparative investigation of the antimicrobial activity of PADMA 28 and selected European herbal drugs.

Weseler A, Saller R, Reichling J.

OBJECTIVE: PADMA 28 is a multicomponent preparation of 20 herbs, calcium sulphate, and camphor, derived from Tibetan medicine. It is usually used in the treatment of peripheral circulatory disorders, accompanied by the symptoms tingling, formication, heaviness and tenseness in arms and legs, numbness in hands and feet, and cramps in the calf. Recently, the question of whether appropriate preparations of PADMA 28 also exhibit antibacterial and antimycotic activity has often been raised. As there are as yet no experimental findings that answer this question, an in vitro study was carried out. In a parallel survey we investigated the antimicrobial properties of 5 herbal drugs which are commonly used in the traditional European folk medicine for the topical treatment of mild skin infections, wounds and eczematous skin lesions. METHODS: The minimum inhibitory concentrations (MIC) and the minimum bactericidal concentrations (MBC) of alcohol-based (tinctures) and aqueous (teas) herbal drug preparations were determined in vitro by a broth microdilution method for 5 Gram-positive and 5 Gram-negative bacteria, as well as the yeast *Candida albicans*. RESULTS: The aqueous and alcohol-based PADMA 28 preparations as well as the corresponding preparations of the European herbal drugs showed an antibacterial effect against Gram-positive bacteria in vitro. These bacteria revealed a somewhat higher sensitivity to the teas prepared from the European herbal drugs (MIC: 1.3-20.0 mg/ml) than to the aqueous preparations of PADMA 28 (MIC: 5.0-40.0 mg/ml). The better antibacterial activity of the European herbal drugs is probably based on their relatively high amount of tanning agents. On the other hand, all tested plant preparations inhibited not at all or only insufficiently the growth of the Gram-negative bacteria tested and that of *Candida albicans*. The ethanolic PADMA 28 tinctures showed an improved inhibitory effect on the Gram-positive bacteria (MIC: 0.38-1.51% tincture or 0.38-1.51 mg PADMA 28/ml) compared with the aqueous preparations; this effect is comparable to the ethanolic tinctures of the tested European herbal drugs (MIC: 0.4-

1.6/3.2% tincture or 0.4-1.6/3.2 mg herbal drug/ml). CONCLUSION: All tested tea preparations and alcoholic tinctures of PADMA 28 as well as those of the selected European herbal drugs exhibited evident antibacterial effects against Gram-positive bacteria in vitro. On the other hand, except for *Klebsiella pneumoniae*, all Gram-negative bacteria tested and the yeast *Candida albicans* were insensitive against the different aqueous and alcohol-based plant extracts.

Digestion. 2002;65:161-71.

A novel treatment for constipation-predominant irritable bowel syndrome using Padma Lax, a Tibetan herbal formula.

Sallon S, Ben-Arye E, Davidson R, Shapiro H, Ginsberg G, Ligumsky M.

BACKGROUND AND AIMS: Padma Lax, a complex Tibetan herbal formula for constipation was evaluated for safety and effectiveness in treating constipation-predominant irritable bowel syndrome in a 3-month double-blind randomised pilot study. METHODS: Patients were recruited from Hadassah Hospital's Gastroenterology clinic, using the Rome I Criteria for irritable bowel syndrome, and the international consensus criteria for constipation. Symptom severity was evaluated monthly by patients and gastroenterologist, using categorical and numerical rating scales. A patient diary recorded daily stool habit and trial medication. RESULTS: In 61 patients, (34 Padma Lax, 27 placebo), significant improvement was demonstrated after 3 months in the Padma Lax group compared to placebo in constipation, severity of abdominal pain, and its effect on daily activities, incomplete evacuation, abdominal distension and flatus/flatulence. A global assessment indicated that significantly more Padma Lax patients, compared to placebo, rated the current treatment superior to previous therapies tried for irritable bowel. Laboratory parameters displayed no clinically significant changes. Side effects, primarily loose stools in 7 Padma Lax patients responded well to lowering treatment dosage from 2 to 1 capsule/day. CONCLUSIONS: Padma Lax is a safe and effective treatment for constipation-predominant irritable bowel syndrome and may offer an alternative to the current multi drug approach. Copyright 2002 S. Karger AG, Basel

Diabetes Care. 2001;24:175-6.

Efficacy of Tibetan medicine as an adjunct in the treatment of type 2 diabetes.

Namdul T, Sood A, Ramakrishnan L, Pandey RM, Moorthy D.

[no abstract available]

Can. J. Physiol. Pharmacol. 2000;78:861-6.

Inhibition of inducible nitric oxide synthesis by the herbal preparation Padma 28 in macrophage cell line.

Moeslinger T, Friedl R, Volf I, Brunner M, Koller E, Spieckermann PG.

Padma 28 is a mixture of herbs used in traditional Tibetan medicine with anti-inflammatory activities. We investigated the effects of Padma 28 on nitric oxide (NO) production by the inducible nitric oxide synthase (iNOS) in lipopolysaccharide stimulated mouse macrophages (RAW 264.7). Padma 28 (0-900 microg/mL) induced a concentration dependent inhibition of inducible nitric oxide synthesis. iNOS protein expression showed a concentration dependent reduction as revealed by immunoblotting when cells were incubated with increasing amounts of Padma 28. Padma 28 decreased iNOS mRNA levels as shown by RT-PCR. Aqueous extracts from *costi amari radix* (*costus* root, the dried root of *Saussurea lappa*) and the outer cover of *myrobalani fructus* (the dried fruit of *Terminalia chebula*), constituents of the complex herb preparation Padma 28, were found to inhibit inducible nitric oxide synthesis by decreasing iNOS protein and iNOS mRNA levels. The inhibition of inducible nitric oxide synthesis might contribute to the anti-inflammatory activities of Padma 28.

Redox Rep. 2000;5:17-22.

Anti- and pro-oxidative properties of PADMA 28, a Tibetan herbal formulation.

Suter M, Richter C.

There is growing public interest in traditional medicine. PADMA 28, a multicomponent herbal preparation derived from Tibetan medicine, has proven efficacy in some clinical trials and tests at the cellular level. We report here on studies of PADMA 28 at the molecular level. Extracts of PADMA 28 contain both reducing and metal ion-chelating substances. In this way, PADMA 28 acts as a powerful antioxidant or prooxidant, depending on its concentration and the reaction under study.

Inflammopharmacology. 1999;7:47-62.

PADMA-28, a traditional tibetan herbal preparation inhibits the respiratory burst in human neutrophils, the killing of epithelial cells by mixtures of oxidants and pro-inflammatory agonists and peroxidation of lipids.

Ginsburg I, Sadovnik M, Sallon S, Milo-Goldzweig I, Mechoulam R, Breuer A, Gibbs D, Varani J, Roberts S, Cleator E, Singh N.

Both aqueous and methanolic fractions derived from the Tibetan preparation PADMA-28 (a mixture of 22 plants) used as an anti-atherosclerotic agent, and which is non-cytolytic to a variety of mammalian cells, were found to strongly inhibit (1) the killing of epithelial cells in culture induced by 'cocktails' comprising oxidants, membrane perforating agents and proteinases; (2) the generation of luminol-dependent chemiluminescence in human neutrophils stimulated by opsonized bacteria; (3) the peroxidation of intralipid (a preparation rich in phospholipids) induced in the presence of copper; and (4) the activity of neutrophil elastase. It is proposed that PADMA-28 might prove beneficial for the prevention of cell damage induced by synergism among pro-inflammatory agonists which is central in the initiation of tissue destruction in inflammatory and infectious conditions.

Phytother Res. 1999;13:218-21.

The therapeutic effect of an herbal formula Badmaev 28 (padma 28) on experimental allergic encephalomyelitis (EAE) in SJL/J mice.

Badmaev V, Kozlowski PB, Schuller-Levis GB, Wisniewski HM.

A herbal formula, Badmaev 28, was evaluated in the treatment of an induced attack in a chronic relapsing model of experimental allergic encephalomyelitis (EAE) in SJL/J mice. Chronic EAE was induced by immunization of 8 week old mice with an emulsion of syngeneic spinal cords with incomplete Freund's adjuvant supplemented with Mycobacterium tuberculosis. Therapy with Badmaev 28 was started on day 25 after the immunization, and the formula was administered in the drinking water at doses of 7, 21, 83 and 166 mg/kg/day. The treatment resulted in significantly decreased mortality compared with the untreated control animals and the therapeutic effect occurred in one experiment in a dose-dependent fashion. Based on the experimental results it is difficult to name one particular mechanism responsible for the therapeutic effectiveness of the formula in the EAE model. Rather this protective effect could be explained by a broad protective mechanism of action discussed in the literature as nonspecific resistance (NSR) to the diversified biological and psychological stressors. The increase in NSR characterizes the action of pharmacological compounds termed adaptogens or bioprotectants.

Soc Sci Med. 1997;44:535-9.

Efficacy of the Tibetan treatment for arthritis.

Ryan M.

Tibetans in the refugee communities in Northern India are exposed to both traditional Tibetan and Western medicine. For Tibetans suffering from arthritis (or trung-bo), the Tibetan treatment was compared with the Western treatment in an open randomized controlled trial. On a significance level of 0.0005, this trial demonstrated that for these Tibetans, their indigenous treatment worked better than the Western treatment for improved limb mobility.

Zhongguo Zhong Xi Yi Jie He Za Zhi. 1995;15:231-3.

[Effect of Tibetan compound prescription on cardiac haemodynamics in experimental myocardial ischemia in dogs]. Article in Chinese

Zhang YJ, Hou Y, Cao YB.

35 healthy and hybrid dogs were divided into the control group (5 dogs), ischemic group (15 dogs) and medicated group (15 dogs). The myocardial ischemia model was produced by ligating the left coronary artery between the branch 2 and 3 among the anterior descending branches. The effect of the herbs on the experimental myocardial ischemia was observed by measuring the Mean Artery Pressure (MAP), the Left Ventricular End Diastolic Pressure (LVEDP), the Heart Rate (HR), the Cardiac Output (CO) and the Cardiac Index (CI) etc. The results showed that the LVEDP was significantly increased and the MAP, the CO and the CI were lowered during the period of myocardial ischemia, which indicated the disorder of cardiac haemodynamics after the myocardial ischemia. By taking the medicine through the duodenum in the medicated group, the CO was obviously increased during the period of myocardial ischemia and also the CI was elevated prominently. The investigation indicated that the medicine could reinforce the cardiac pump function and adjust the disorder of cardiac haemodynamics resulted from myocardial ischemia.

J Clin Lab Immunol. 1995;46:13-23.

The effect of Padma-28, a traditional Tibetan herbal preparation, on human neutrophil function.

Matzner Y, Sallon S.

Human neutrophils were studied in vitro in the presence of the herbal preparation Padma-28. At concentrations higher than 0.3 mg/ml, the Padma-28 induced O₂⁻ production in unstimulated neutrophils. At lower concentrations, O₂⁻ production was inhibited in phorbol myristate acetate (PMA) stimulated cells. Lysozyme release by PMA and opsonized zymosan-stimulated cells was inhibited by Padma-28 at a concentration dependent manner. On the other hand, random and directed migration and adhesion to nylon fibers were not affected. These results suggest that Padma-28 may have anti-inflammatory activity whose mechanism remains to be elucidated.

Ugeskr. Laeg. 1994;156:6207-9.

[Padma-28, a herbal preparation, increases walking distance in patients with intermittent claudication]
Article in Danish

Drabaek H, Mehlsen J, Petersen JR, Himmelstrup H, Hansen KF.

Thirty-six patients with stable intermittent claudication were randomized in a doubleblind study either to treatment with two tablets of Padma-28 twice daily (containing 340 mg dried herbal mixture composed according to an ancient lamaistic prescription) or placebo for four months. Effect of treatment was quantified by measurements of systemic and peripheral systolic blood pressures, and pain-free and maximal walking distances on a tread-mill. The actively treated group attained a significant increase in pain-free walking distance from 115 m (72-218) to 227 m (73- >1000, p < 0.05). The placebo group did not show significant changes in

either pain-free or maximal walking distance. Significant changes in systemic or peripheral blood pressures could not be demonstrated in any of the groups. In conclusion, our study has shown that treatment with Padma-28 over a four month period significantly increases the walking distance in patients with stable intermittent claudication of long duration.

Angiology. 1993;44:863-7.

A botanical compound, Padma 28, increases walking distance in stable intermittent claudication.

Drabaek H, Mehlsen J, Himmelstrup H, Winther K.

Thirty-six patients with a median age of sixty-seven years and a median duration of intermittent claudication of five years were randomized to either active treatment with Padma 28 or placebo. The effect of treatment was quantified by measurements of systemic and peripheral systolic blood pressures and by measurements of the pain-free and the maximal walking distance on a treadmill. The ankle pressure index (ankle systolic pressure/arm systolic pressure) was calculated. The group randomized to active treatment received two tablets bid containing 340 mg of a dried herbal mixture composed according to an ancient lamaistic preparation (Padma 28). After active treatments, administered over a period of four months in a double-blinded, randomized design, the patients allocated to this group attained a significant increase in the pain-free walking distance from 52 m (20-106) to 86 m (24-164; $P < 0.05$) and in the maximal walking distance from 115 m (72-218) to 227 m (73- > 1,000; $P < 0.05$). The patient-group receiving placebo treatments did not show any significant changes in either the painfree or the maximal walking distance. The authors could not demonstrate any significant changes in the ankle pressure index either during active or during placebo treatment. In conclusion, this study has shown that treatment with Padma 28 over a period of four months significantly increased the walking distance in patients with stable, intermittent claudication of long duration.

Zhongguo Zhong Xi Yi Jie He Za Zhi. 1993;13:467-70, 452-3.

[Immune function of rheumatoid arthritis treated by medicated-bath therapy in Tibetan medicine] Article in Chinese

Zhao SL, Geng PL, Sang J.

The changes of the immune function of rheumatoid arthritis before and after the Tibetan medicated-bath was observed. It showed a higher level of the rheumatoid factor (RF) titre, immunoglobulin (Ig) G, M, A and CD4 cells, but the CD8 cells was obviously lower before the treatment. Clinical data indicated that the medicated-bath had significant effective rate. In order to elucidate the mechanism of the medicated-bath upon rheumatoid arthritis the RF titre, Ig level, complement C3, 3H-TdR incorporated with lymphocytes transformation and CD3, CD4, CD8 cell level were assayed. Results showed that RF titre decreased after the bath and the negative transforming rate reached 70.6%, Ig level obviously dropped as well as the number of CD4 cells while CD8 cell level increased. The transforming stimulation index of lymphocyte cells obviously decreased. All of the above mentioned showed that there was a higher concentration of the enhancing factor of interleukin-2 (IL2-EF) involved in lymphocyte culture of rheumatoid arthritis patients. They suggested that the Tibetan medicated-bath had an immunomodulating effect on rheumatoid arthritis patients through increasing the level of CD8 cells and reducing CD4 cells.

Arch. Immunol. Ther. Exp. (Warsz.). 1992;40:291-5.

Padma 28 modifies immunological functions in experimental atherosclerosis in rabbits.

Giełdanowski J, Dutkiewicz T, Samochovec L, Wójcicki J.

The effect of Padma 28 on selected parameters of humoral and cellular immune reactions in rabbits subjected to experimental atherosclerosis was studied. The drug significantly reduced the size of atherosclerotic plaques in the aorta and restored to a varying extent the immune functions studied. The possible mechanism by which Padma 28 may exert its anti-atherosclerotic action is discussed in the scope of the immunological theory of atherosclerosis.

Ann Acad Med Stetin. 1991;37:191-202.

[Treatment of chronic ischemia of the lower extremities with complex herbal preparation] Article in Polish

Smulski HS.

Chronic ischemia of the lower extremities with atherosclerosis background is being manifested by intermittent claudication. For treating the intermittent claudication many drugs are used, which may give rise to therapeutical side effects. In 50 patients with diagnosed arteriosclerosis affecting the lower extremities in II stage according to Fontain, a vegetable preparation PADMA-28 was applied for 16 weeks. A marked, statistically significant elongation of the claudication distance was achieved. That was measured, under standardized condition, on an ergometer-treadmill. Moreover, there was also a decrease in the index of blood platelets aggregation, a drop in the level of cholesterol, triglycerides, total lipids, beta lipoproteins, and an increase in ++alpha lipoproteins. Also 50 patients were receiving placebo for 16 weeks, but no positive results were observed in comparison with preparation PADMA-28. The studies were carried out by the method of double blind test, the latter was accomplished by randomized method. Observation, the performed biochemical examinations did not reveal any undesirable effect. Drug tolerance was excellent. The positive influence of the drug may result from summed action of components contained in the preparation namely: bioflavonoides, salicylates, valepotriates, tannins, phenol acids, ethereal oils and esters of acids. PADMA-28 may be a useful adjuvant to therapeutic methods with regard to chronic ischemia of the lower extremities in II stage, according to Fontain.

Acta Physiol Pol. 1989;40:387-92.

Inhibition of ethanol-induced changes in rats by Padma 28.

Wójcicki J, Samochowiec L, Kadłubowska D.

In male Wistar rats the protective effect of Padma 28 against changes induced by prolonged treatment with ethyl alcohol was investigated. Exposure of the animals to prolonged ethyl alcohol consumption caused a significant increase in AspAT (by 32%), A1AT (by 50%) and alkaline phosphatase (by 372%) activities as well as an increase in the levels of bilirubin (by 98%) and lipids in the blood serum and lipids in the liver homogenate. Padma 28 administration was found to exert a protective action against these changes: a significant reduction of blood total lipid, triacylglycerol, total cholesterol and bilirubin concentrations as well as in the activity of the liver enzymes was observed.

Arch Immunol Ther Exp (Warsz). 1987;35:289-302.

Immunostimulation in recurrent respiratory tract infections therapy in children.

Prusek W, Jankowski A, Radomska G, Wieczorek E, Podwysocka M.

Selected immunologic parameters and effectivity of immunotherapy was evaluated in 117 children (12-month-10-year-1-old) suffering from recurrent respiratory tract infections. All the children displayed a profound depression of T lymphocytes number, which resemble the situation seen in AIDS patients. An increase of serum IgM concentration was also noted. Immunotherapy included treatment with the following preparations: TFX and Levamisol which stimulate T cell functions, Broncho-Vaxom which stimulates specific antibody production and a complex herb preparation PADMA showing undefined general stimulatory activity. Separate group of children was subjected to climatotherapy in Czerniawa Sanatorium and received no immunostimulants. All methods of treatment employed had beneficial effect. The highest percentage of positive results was obtained in children receiving TFX and Levamisol. In all groups under study, an elevation of T cells percentage was observed. This was especially evident in Levamisol treated patients. There was no correlation, however, between T cells number and clinical improvement.

Schweiz Med Wochenschr. 1985;115:752-6.

[Effects of the Tibetan herbal preparation Padma 28 in intermittent claudication] Article in German

Schräder R, Nachbur B, Mahler F.

In a placebo-controlled double blind study the effect of Padma 28, a Tibetan herbal prescription, on patients with intermittent claudication was investigated. After two weeks without vasoactive therapy 23 patients were treated by Padma 28 and 20 by placebo. The patients had a disease history of at least 8 months, a steady state for symptoms (maximum walking distance below 250 m), and were distributed randomly in the two groups. After 16 weeks the patients treated with Padma 28 exhibited on standardized ergometry an increase of some 100% (p less than 0.01) in the maximum as well as painfree walking distance. The control patients showed increases of 21% in maximum (p less than 0.05 as compared to Padma 28), and 46% in painfree walking distance. The drug was well tolerated and no drop-out ensued because of side effects.

Schweiz Rundsch Med Prax. 1978;67:1407-9.

[A lamaistic formula for the treatment of peripheral arterial occlusive diseases (author's transl)] Article in German

Hürlimann F.

ABSTRACT: Despite extensive research, many questions concerning the treatment of peripheral arterial occlusive diseases remain unanswered. The herbal mixture PADMA 28 is not a vasodilator. The evident main effect comes from the inhibition of the platelet aggregation induced by collagen. Therefore it seemed to be of interest to check this lamaistic formula for the treatment of peripheral arterial occlusive diseases as to its clinical effectiveness. The following results were shown: 1. In the cases of fully trained patients suffering from stage II (type of pelvis/femur-occlusion) PADMA 28 significantly lengthens the pain free walking distance. 2. As to the circulation of the blood in the calf, neither amelioration nor deterioration could be found (measured with venous obstruction plethysmography). 3. PADMA 28 improved nightly cramps, paresthesia and signs of "restless legs". 4. The improvement in nutritive blood flow caused by PADMA 28 can be deduced from the decline of pain at rest in patients suffering from peripheral occlusive diseases stage III and IV. 5. There were no side effects. Neither contraindications could be found, nor was there incompatibility with conventional medicaments simultaneously taken, such as anticoagulant, antidiabetic, antihypertensive, antilipemic and digitalis drugs. 6. PADMA 28 is a herbal mixture of the lamaistic medical science. It is a genuine alternative to existing vasoactive substances, perorally taken.

Schweiz Rundsch Med Prax. 1970;59:1190-3.

[A lamaistic prescription-formula for the treatment of chronic constipation] Article in German

Flück H, Bubb WP.

No abstract available.