

Research Highlights

EXTRACELLULAR MATRIX IS A POTENTIAL THERAPEUTIC TARGET OF *ARNICA MONTANA* DURING HEALING

Article title: Fibronectin gene up-regulation by *Arnica montana* in human macrophages: Validation by real-time polymerase chain reaction assay

Authors: Marta Marzotto, Fabio Arruda-Silva, Paolo Bellavite

Journal: Homeopathy 2020;109(03):140-145. Doi: 10.1055/s-0040-1708044.

Summary: *Arnica montana* L. is a popular traditional medicine used for its therapeutic properties in healing traumas, but little is known about its biological action on tissue formation and repair. This new work tested the effects of *Arnica montana* L. homeopathic dilutions on human macrophages, key cells in tissue defence and repair. Macrophages derived from the THP-1 cell line were differentiated with interleukin-4 to induce a 'wound-healing'-like phenotype, and treated with various dilutions of *Arnica montana* L. centesimal dilutions (2c, 3c, 5c, 9c and 15c) or control solvent for 24 h. RNA samples from cultured cells were analysed by real-time quantitative polymerase chain reaction in five separate experiments. *Arnica montana* L. at the 2c dilution (final concentration of sesquiterpene lactones in cell culture = 10^{-8} mol/L) significantly stimulated the expression of three genes which code for regulatory proteins of the extracellular matrix, namely FN1 (fibronectin 1, % increase of $21.8 \pm$ standard error of the mean 4.6), low-density lipoprotein receptor-related protein 1 (% increase of 33.4 ± 6.1) and heparan sulphate proteoglycan 2 (% increase of 21.6 ± 9.1). Among these genes, the most quantitatively expressed was FN1. In addition, FN1, unlike other candidate genes, was upregulated in cells treated with higher dilutions/dynamisations (3c, 5c and 15c) of *Arnica montana* L.

Comment: The results support evidence that the extracellular matrix is a potential therapeutic target of *Arnica montana* L., with positive effects on cell adhesion and migration during tissue development and healing. Hence, it seems that *Arnica montana* L. impacts a network of biological functions including inflammation and extracellular matrix regulation.

REVIEW OF EFFECTS OF HIGHLY DILUTED DRUGS ON *TRYPANOSOMA CRUZI* INFECTION

Article title: Effects of highly diluted drugs on experimental infection with *Trypanosoma cruzi* in vivo: A systematic review

Authors: Daniela Cristina Grégio d'Arce Mota, Érika Cristina Ferreira, Fabiana Nabarro Ferraz, Maria Vitória Felipe de Souza, Bruna Lauton Simões, Denise Lessa Aleixo, Jorge Juarez Vieira Teixeira, Silvana Marques de Araújo

Journal: J Altern Complement Med 2020 Oct;26(10):866-883. Doi: 10.1089/acm.2019.0472.

Summary: The effects of the use of highly diluted drugs in the treatment of experimental infection with *Trypanosoma cruzi* were investigated through a systematic review. The authors searched for scientific publications in the databases from 2000 to 2018, following the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement. According to the criteria established, a total of 22 studies were included. The study took place at the State University of Maringá, Maringá, PR, Brazil. Male mice (*Mus musculus*) or rats (*Rattus norvegicus*) were the subjects of the study. Interventions were highly diluted drugs. For outcome measures, the parameters evaluated in the studies were parasitological, clinical, immunological, histopathological and haematological. The studies demonstrated that the effects of highly diluted drugs are related to their dynamisations, treatment regimen and host susceptibility to *T. cruzi* infection, and depend on the initial information transmitted to the treated organism, making this information the 'model' of how the treated organism will react. Regardless of the mechanism of action, these drugs provide a decrease in inflammation, which is one of the central phenomena of the pathogenesis of *T. cruzi* infection.

Comment: This systematic review brings out the importance of the *T. cruzi* infection model as a reliable and valid model for studying different effects produced by highly diluted drugs. This study contributes to considering these drugs as a possible way of dealing with "treatment" in general, presents the need to reexamine the biochemical model and develop a model for the effect of high dilutions in general, as well as for the treatment of parasitic infections.

INDIVIDUALISED HOMOEOPATHIC TREATMENT MAY BE HELPFUL IN PITUITARY ADENOMAS WITH INCREASED RISK OF INTRASELLAR HAEMORRHAGE

Article title: Pituitary microadenoma treated with individualized homeopathic medicine: A case report

Authors: Mohit Mathur

Journal: Homeopathy 2020;109(04):243-247. Doi: 10.1055/s-0040-1713383.

Summary: Pituitary adenomas are common benign tumours of the pituitary gland with an overall estimated prevalence of 16.7%. As per the revised World Health Organization classification, these tumours are identified by their histological subtypes and are designated by their pituitary cell lineage instead of the hormone they produce. The lactotroph adenoma is the most common subtype of hormone-producing

pituitary adenoma. Surgery is the mainstay of treatment, but complications are encountered. So far, there is no reported study evaluating individualised homeopathic intervention in pituitary adenoma in peer-reviewed journals. This case study describes a case of functional lactotroph microadenoma with a history of failed surgical treatment and heavy intrasellar haemorrhage occurring during the surgery. *Phosphorus* was prescribed as an individualised homeopathic medicine on the basis of symptoms – haemorrhagic complication during surgical procedure and aggravation of headache thereafter. There was a marked subjective improvement along with complete tumour regression, as evidenced by repeat magnetic resonance imaging scans. The Modified Naranjo Criteria total score was +10 out of a possible +13, providing some evidence to attribute the clinical outcome with the homeopathic intervention.

Comment: This case study reconfirms the association between increased frequency of headaches and pituitary haemorrhage among cases of lactotroph adenoma. It also suggests that individualised homeopathic treatment may be helpful in pituitary adenomas with increased risk of complications such as intrasellar haemorrhage.

PROLONGED PATIENT SURVIVAL AND IMPROVED QUALITY OF LIFE WITH ADDITIVE HOMOEOPATHY IN PATIENTS WITH NON-SMALL CELL LUNG CANCER

Article title: Homeopathic treatment as an add-on therapy may improve quality of life and prolong survival in patients with non-small cell lung cancer: A prospective, randomized, placebo-controlled, double-blind, three-arm, multicenter study

Authors: Michael Frass, Peter Lechleitner, Christa Gründling, Claudia Pirker, Erwin Grasmuk-Siegl, Julian Domayer, Maximilian Hochmair, Katharina Gaertner, Cornelia Duscheck, Ilse Muchitsch, Christine Marosi, Michael Schumacher, Sabine Zöchbauer-Müller, Raj K Manchanda, Andrea Schrott, Otto Burghuber

Journal: *Oncologist* 2020 Oct 3. Doi: 10.1002/onco.13548. Online ahead of print.

Summary: Patients with advanced non-small cell lung cancer (NSCLC) have limited treatment options. Alongside conventional anticancer treatment, additive Homoeopathy might help to alleviate the side effects of conventional therapy. The aim of the present study was to investigate whether additive Homoeopathy might influence the quality of life (QoL) and survival in patients with NSCLC. In this prospective, randomised, placebo-controlled, double-blind, three-arm, multicentric, Phase III study, the possible effects of additive homeopathic treatment were evaluated compared with placebo in patients with Stage IV NSCLC, with respect to QoL in the two randomised groups and survival time in all the three groups. Treated patients visited the outpatients' centres every 9 weeks: 150 patients with Stage IV NSCLC

were included in the study; 98 received either individualised homeopathic remedies ($n = 51$) or placebo ($n = 47$) in a double-blinded fashion and 52 control patients without any homeopathic treatment were observed for survival only. The constituents of the different homeopathic remedies were mainly of plant, mineral or animal origin. The remedies were manufactured by step-wise dilution and succussion, thereby preparing stable Good Manufacturing Practice-grade formulations. QoL as well as functional and symptom scales showed a significant improvement in the Homoeopathy group when compared with that of placebo after 9 and 18 weeks of homeopathic treatment ($P < 0.001$). The median survival time was statistically significantly longer in the Homoeopathy group (435 days) versus placebo (257 days; $P = 0.010$) as well as versus control (228 days; $P < 0.001$). Survival rate in the Homoeopathy group differed statistically significantly from placebo ($P = 0.020$) and from controls ($P < 0.001$).

Comment: Conventional medicine and Homoeopathy work well together. In this study, QoL and survival improved with additive Homoeopathy in patients with NSCLC.

DIABETES LEADS TO A TWOFOLD INCREASE IN THE ODDS OF SEVERE CORONAVIRUS DISEASE AND ASSOCIATED MORTALITY

Article title: Diabetes mellitus association with coronavirus disease 2019 (COVID-19) severity and mortality: A pooled analysis

Authors: Gaurav Aggarwal, Giuseppe Lippi, Carl J Lavie, Brandon Michael Henry, Fabian Sanchis-Goma

Journal: *J Diabetes* 2020 Nov;12(11):851-855. Doi: 10.1111/1753-0407.13091.

Summary: Because the prevalence of diabetes mellitus (DM) has been reported to be high among coronavirus disease 2019 (COVID-19) patients, a pooled analysis of current studies for evaluating potential associations between DM and infection severity outcomes in COVID-19 patients was carried out. Databases were searched for studies published until 31 March 2020. A meta-analysis was performed to estimate the odds ratio (OR) and 95% confidence interval (CI) of DM in COVID-19 patients with or without severe disease and in non-survivors versus survivors. The statistical analysis was carried out using inverse-variance model. Finally, a random-effects meta-regression using log was performed or the impact of mean age and gender on the association of DM with disease severity and mortality in patients with COVID-19 was evaluated. The final pooled analysis included 16 studies. Twelve studies reported a history of DM in severe versus non-severe cases, with a sample of 2564 confirmed COVID-19 patients (754, 29.4% being severe cases). A total of 265 patients (10.3%) were classified as having a history of DM. Four studies with 618 patients (307, 42.5% of non-survivors) compared the rate of DM between survivors and non-surviving

COVID-19 patients, of which 96 (15.5%) were previously diagnosed with DM. COVID-19 patients previously diagnosed with DM were found to be associated with a statistically significant increased risk of worse COVID-19 infection (OR: 2.60 [95% CI: 1.96 to 3.45], $I^2 = 56\%$, Cochran's $Q = 24.9$, $P = 0.01$). In the pooled analysis of the four studies reporting mortality data, a significant association was found with increased risk of mortality in COVID-19 patients previously diagnosed with DM (OR: 2.03 [95% CI: 1.29–3.20], $I^2 = 0\%$, Cochran's $Q = 2.63$, $P = 0.45$). A meta-regression analysis showed no effect of age or gender on the association of DM with COVID-19 infection severity or mortality. There were ~twofold increased odds of severe COVID-19 and a ~twofold increased risk of odds of mortality in patients with a history of DM compared to those without DM.

Comment: As with the association of DM, there is a twofold increase in the odds of severe coronavirus disease and associated mortality. Thus, patients with a history of DM should be closely monitored if they get infected with COVID-19. They should be treated with increased caution, and close monitoring of the blood sugar levels can improve treatment outcomes in such patients.

DEPRESSION AND POST-TRAUMATIC STRESS DISORDER ARE MAJOR MENTAL HEALTH MANIFESTATIONS IN SNAKEBITE SURVIVORS

Article title: Mental health conditions after snakebite: A scoping review

Authors: Soumyadeep Bhaumik, Sudha Kallakuri, Amanpreet Kaur, Siddhardha Devarapalli, Mercian Daniel

Journal: BMJ Global Health 2020;5, no. 11. Doi: <https://doi.org/10.1136/bmjgh-2020-004131>

Summary: Snakebite is a neglected tropical disease. Snakebite causes at least 120,000 deaths each year, and it is estimated that there are three times as many amputations. Snakebite survivors are known to suffer from long-term physical and psychological sequelae, but not much is known on the mental health manifestations post snakebite. A scoping review was conducted; electronic databases were searched (experts were contacted and reference screening was conducted to identify primary studies on mental health manifestations after snakebite envenomation). Two reviewers independently conducted title and abstract screening as well as full-text evaluation for final inclusion decision. The data were extracted as per a standardised form and narrative synthesis was conducted. A total of 334 studies were retrieved and finally 11 studies were included that met the eligibility criteria. Of the 11 studies reported, post-traumatic stress disorder (PTSD) was the most commonly studied mental health condition after snakebite, with five studies reporting it. Estimate of the burden of PTSD after snakebite was available from a modelling study. The other mental health conditions reported were focused

on depression, psychosocial impairment of survivors after a snakebite envenomation, hysteria, delusional disorders and acute stress disorders.

Comment: There is a need for more research on understanding the neglected aspect of psychological morbidity of snakebite envenomation, particularly in countries with high burden. From the limited evidence available, depression and PTSD are major mental health manifestations in snakebite survivors. Homoeopathically, history of snakebites may be emphasised while treating the aforesaid conditions. Further, homoeopathic medicines derived from snakes can be used for the treatment of depression with a positive history of snakebites.

RED MEAT CONSUMPTION IN PREGNANCY MAY PREDISPOSE TO THE DEVELOPMENT OF GESTATIONAL DIABETES MELLITUS

Article title: Food habits in pregnancy and its association with gestational diabetes mellitus: Results from a prospective cohort study in public hospitals of urban India

Authors: R. Deepa, Melissa Glenda Lewis, Onno C. P. Van Schayck and Giridhara R. Babu

Journal: BMC Nutrition 2020;6:63. Doi: <https://doi.org/10.1186/s40795-020-00388-x>.

Summary: Few studies have explored the relationship between food habits and the risk of gestational diabetes mellitus (GDM) in women from India. The aim of the study was to investigate the association of food habits with the risk of GDM. As part of the MAASTHI prospective cohort study in urban Bengaluru, India, pregnant women aged between 18 and 45 years, less than 36 weeks of gestation, were included. During baseline, the participants' age, education, physical activity levels and food habits were recorded. Screening of GDM was done by the World Health Organization diagnostic criteria using a 2-h 75-g oral glucose tolerance test between the 24th and 36th weeks of gestation. A total of 1777 pregnant women were included in the study. The study showed that 17.6% of the women had GDM, of which 76.7% consumed red meat. Red meat consumption was associated with an increased risk of GDM adjusted relative risk (aRR = 2.1, 95% CI: 1.5, 2.9) after adjusting for age, family history of diabetes and socioeconomic status.

Comment: High intake of red meat in pregnancy needs further examination. Furthermore, future studies should consider evaluating the risk of red meat consumption against the combined effect of inadequate consumption of vegetables, fruits and dairy products in pregnant women. Interventions to educate women belonging to lower socioeconomic status on inexpensive, seasonal and healthy food might be helpful.

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Conflicts of interest

None declared.

Jain: Research updates

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