

Research at a Glance

RESEARCH AT A GLANCE

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COMPILED & EDITED

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PREFACE

Introduction

The library of the Central Council for Research in Homoeopathy has been circulating "Research at a Glance". The main objective is to disseminate precise information/citation about scientific articles published in various journals/magazine other than the journals subscribed by this Council.

Scope

This volume covers articles on Homeopathy, Ayurveda, Unani, Yoga.

Arrangement of Entries

The articles are indexed under the name of the authors, arranged in alphabetical order. The entries have been made in the following order:

Author

Title

Name of Journal

year of publication; Volume (issue no.): pagination

Abstract

Acknowledgement

We are grateful to Dr. Subhash Kaushik, Director General, CCRH for his encouragement and valuable suggestions from time to time. We sincerely acknowledge the cooperation of Mrs. Nisha Adhikari, Office Assistant in compiling this bulletin.

(Dr. O.P. Verma)
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HOMOEOPATHY

Gaertner K, Teut M, Walach H. Homeopathy effective for attention deficit and hyperactivity disorder? A meta-analysis. *Pediatr Res.* 2022 Jun 14. doi: 10.1038/s41390-022-02127-3. Online ahead of print. PMID: 35701608

Abstract:

Background: Attention deficit and hyperactivity disorder (ADHD) prevalence is increasing, compliance to treatment is often poor, and additional treatment options are warranted. We aim to investigate whether individualized homeopathic treatment is effective in children with ADHD when compared to placebo or usual care alone.

Methods: Thirty-seven online sources were searched with a last update in March 2021. Studies investigating the effects of individualized homeopathy against any control in ADHD (ICD-10 category F90.0) were eligible. Data were extracted to a predefined excel sheet independently by two reviewers.

Results: Six studies were analyzed. All but one were randomized and showed low-to-moderate risk of bias; two were controlled against standard treatment and four were placebo-controlled and double-blinded. The meta-analysis revealed a significant effect size across studies of Hedges' $g = 0.542$ (95% CI 0.311-0.772; $z = 4.61$; $p < 0.001$) against any control and of $g = 0.605$ (95% CI 0.05-1.16; $z = 2.16$, $p = 0.03$) against placebo ($n = 4$). The effect estimations are based on studies with an average sample size of 52 participants.

Conclusions: Individualized homeopathy showed a clinically relevant and statistically robust effect in the treatment of ADHD.

Impact: This paper summarizes the current evidence of individualized homeopathy in attention deficit and hyperactivity disorder (ADHD), and the results show a clinical improvement for patients receiving this additional treatment. Individualized homeopathy has shown evidence of effectiveness in the treatment of ADHD in several small trials, this is the first systematic review and meta-analysis. This data may encourage caregivers to consider co-treatment or referral to individualized homeopathy when treating childhood ADHD.

AYURVEDA

Ahmad A, Khan MU, Aslani P. Patient preferences for the treatment of type 2 diabetes in Australia: a discrete choice experiment. J Diabetes Metab Disord. 2022 Jan 27;21(1):229-240. doi: 10.1007/s40200-021-00962-5. eCollection 2022 Jun. PMID: 35673490

Abstract:

Background: Australia has a high proportion of migrants, with an increasing migration rate from India. Type 2 diabetes is a chronic condition common amongst the Indian population. The decision to initiate and continue medication therapy (conventional or ayurvedic medicine) is complex and is influenced by a wide range of factors.

Objective: To determine preferences for conventional vs. ayurvedic medicines in Indian migrants with diabetes, and to identify the factors that may influence their preferences.

Methods: A discrete choice experiment was conducted with participants in Australia who were migrants from India with type 2 diabetes (n=141). Each respondent evaluated eight choice tasks consisting of eight attributes describing medicines and outcomes of medication taking; and were asked to choose 'conventional', or 'ayurvedic' medicine. A mixed multinomial logit model was used to estimate preferences.

Results: Overall, respondents' preference to initiate a medicine was negative for both conventional ($\beta=-2.33164$, $p<0.001$) and ayurvedic medicines ($\beta=-3.12181$, $p<0.001$); however, significant heterogeneity was noted in participants' preferences (SD: 2.33122, $p<0.001$). Six significant attributes were identified to influence preferences. In decreasing rank order: occurrence of hypoglycaemic events (relative importance, RI=24.33%), weight change (RI=20.00%), effectiveness of medicine (RI=17.91%), instructions to take with food (RI=17.05%), side effects (RI=13.20%) and formulation (RI=7.49%). Respondents preferred to initiate a medicine despite potential side effects.

Conclusions: There was a greater preference for conventional medicine, though neither were preferred. Medicine attributes and medication-taking outcomes influenced people's preferences for an antidiabetic medicine. It is important to identify individual preferences during healthcare consultations to ensure optimal medication-taking.

Amarasiri SS, Attanayake AP, Mudduwa LKB, Jayatilaka KAPW. Nephroprotective mechanisms of Ambrette (*Abelmoschus moschatus* Medik.) leaf extracts in adriamycin mediated acute kidney injury model of Wistar rats. J Ethnopharmacol. 2022 Jun 28;292:115221. doi: 10.1016/j.jep.2022.115221. Epub 2022 Mar 23. PMID: 35339624

Abstract:

Ethnopharmacological relevance: Ambrette (*Abelmoschus moschatus* Medik., Family: Malvaceae) is a common Ayurvedic herbal medicine used in the treatment of kidney-related diseases, in the forms of tea, medicated oil, medicated wine, etc., however, its nephroprotective mechanisms remain unexploited.

Aim of the study: To investigate the mechanisms by which the hexane (A-HE), ethyl acetate (A-EE), butanol (A-BE), and aqueous (A-WE) leaf extracts of Ambrette protect against the adriamycin-mediated acute kidney injury in Wistar rats.

Materials and methods: A-HE, A-EE, A-BE, A-WE, and fosinopril sodium were administered at therapeutically effective doses (55, 75, 60, 140, 0.09 mg/kg) to adriamycin-induced (5 mg/kg, ip) Wistar rats for 28 consecutive days.

Results: Oral administration of the selected extracts of *A. moschatus* resulted in amelioration of kidney injury as observed by the significant changes of biomarkers of kidney function in serum and in urine, biochemical parameters of oxidative stress, and inflammation in kidney homogenates ($p < 0.05$). Furthermore, the administration of plant extracts caused a significant reduction in total kidney injury scores in H and E stained kidney sections ($p < 0.05$). The immunohistochemical expression of the inflammatory marker, COX-2, and the pro-apoptotic marker, Bax, were attenuated and the expression of the anti-apoptotic marker, BCL-2, was increased. A-HE exerted superior nephroprotective effects over the other three extracts and the drug reference standard.

Conclusions: The findings revealed that Ambrette exerts promising protective effects against adriamycin-mediated acute kidney injury through antioxidant, anti-inflammatory, and anti-apoptosis pathways. A-HE might serve as a potential candidate for the development of therapeutic drug leads that will be beneficial in the treatment of acute kidney injury.

Balakrishnan P, Ajayan S, Mukkudakkattu S, Nechiyl K, Nambi N. Review of unique ophthalmic formulations in Vaidya Manorama: A traditional Kerala Ayurveda literature. J Ayurveda Integr Med. 2022 Jun 2;13(2):100576. doi: 10.1016/j.jaim.2022.100576. Online ahead of print. PMID: 35661934

Abstract:

Vaidya Manorama is a folklore Kerala Ayurveda literature that encompasses time- tested low-budget formulations that can be prepared from easily available resources. Ayurveda Ophthalmology has been described in Chapter

twenty-eight of the literature. Many unique formulations like eating firefly (khadyota), preparing ghee from fresh-water shellfish (tadaka-shuktika), Kadali phala (a special type of banana) bidalaka, dropping of juice of palasha (*Butea monosperma*) into eyes for various clinical conditions are described. We review the unique ophthalmology formulations in this chapter to bring them to limelight. Few herbo-mineral formulations are also described for which toxicity and safety studies are warranted. All these handy formulations may help clinicians in day-to-day practice or may be a lead for novel research.

Balkrishna A, Verma S, Mulay VP, Gupta AK, Haldar S, Varshney A. *Withania somnifera* (L.) Dunal whole-plant extracts exhibited anti-sporotrichotic effects by destabilizing peripheral integrity of *Sporothrix globosa* yeast cells. PLoS Negl Trop Dis. 2022 Jun 17;16(6):e0010484. doi: 10.1371/journal.pntd.0010484. eCollection 2022 Jun. PMID: 35714107

Abstract:

Chronic topical cases of Sporotrichosis, a chronic fungal infection caused by the ubiquitously present cryptic members of the *Sporothrix* species complex, are treated with oral administrations of itraconazole. However, severe pulmonary or disseminated cases require repeated intra-venous doses of amphotericin B or even surgical debridement of the infected tissue. The unavoidable adverse side-effects of the current treatments, besides the growing drug resistance among *Sporothrix* genus, demands exploration of alternative therapeutic options. Medicinal herbs, due to their multi-targeting capacity, are gaining popularity amidst the rising antimicrobial recalcitrance. *Withania somnifera* is a well-known medicinal herb with reported antifungal activities against several pathogenic fungal genera. In this study, the antifungal effect of the whole plant extract of *W. somnifera* (WSWE) has been explored for the first time, against an itraconazole resistant strain of *S. globosa*. WSWE treatment inhibited *S. globosa* yeast form growth in a dose-dependent manner, with IC₅₀ of 1.40 mg/ml. Minimum fungicidal concentration (MFC) was found to be 50 mg/ml. Sorbitol protection and ergosterol binding assays, revealed that anti-sporotrichotic effects of WSWE correlated well with the destabilization of the fungal cell wall and cell membrane. This observation was validated through dose-dependent decrease in overall ergosterol contents in WSWE-treated *S. globosa* cells. Compositional analysis of WSWE through high performance liquid chromatography (HPLC) exhibited the presence of several anti-microbial phytochemicals like withanone, withaferin A, withanolides A and B, and withanoside IV and V. Withanone and withaferin A, purified from WSWE, were 10-20 folds more potent against *S. globosa* than WSWE, thus, suggesting to be the major phytochemicals responsible for the observed anti-sporotrichotic activity. In conclusion, this study has demonstrated the anti-sporotrichotic property of the whole plant extract of *W. somnifera* against *S. globosa* that could be further explored for the development of a natural antifungal agent against chronic Sporotrichosis.

Bhavaniramy S, Sibiya A, Alothaim AS, Al Othaim A, Ramar V, Veluchamy A et al. Evaluating the structural and immune mechanism of Interleukin-6 for the investigation of goat milk peptides as potential treatments for COVID-19. J King Saud Univ Sci. 2022 Jun;34(4):101924. doi: 10.1016/j.jksus.2022.101924. Epub 2022 Feb 25. PMID: 35233153

Abstract:

The function of Immune control, haematopoiesis, and inflammation all depend on the cytokine Interleukin 6 (IL-6), and higher expression of IL-6 is seen in COVID-19 and other diseases. The immune protein IL-6 activation is dependent on binding interactions with IL-6R α , mIL-6R, and sIL-6R for its cellular function. Termination of these reaction could benefit for controlling the over-expression in COVID-19 patients and that may arise as inhibitors for controlling COVID-19. Traditionally, the goat milk has been prescribed as medicine in ayurvedic practice and through this work, we have explored the benefits of peptides from goat milk as IL-6 inhibitors, and it have the potential of inhibiting the over expression of IL-6 and control the COVID-19 disease. Computational experiments have shown that goat peptides had strong interactions with IL-6, with higher scoring profiles and energy efficiency ranging from -6.00 kcal/mol to -9.00 kcal/mol in docking score and -39.00 kcal/mol in binding energy. Especially the YLGYLEQLLR, VLVLDTDYK and AMKPWIQPK peptides from goat milk holds better scoring and shows strong interactions were identified as the most potential IL-6 inhibitor candidates in this study. Peptides from Goat proteins, which are capable of binding to the IL-6 receptor with strong binding conformations, have no negative effects on other immune system proteins.

Damame H, Rooge S, Patil R, Garad C, Arvindekar A. In vitro differentiation of human pancreatic duct-derived PANC-1 cells into β -cell phenotype using *Tinospora cordifolia*. In Vitro Cell Dev Biol Anim. 2022 Jun 6. doi: 10.1007/s11626-022-00690-x. Online ahead of print. PMID: 35668153

Abstract:

Type 1 diabetes mellitus is an autoimmune disorder leading to loss of beta cells. There is a dire need to inhibit apoptosis and induce regeneration of new beta cells. There are plants in the Indian medicine system having the potential for rejuvenation. In the present study, we have attempted to evaluate the capacity of aqueous extract of *Tinospora cordifolia* to regenerate beta cells from PANC-1 ductal cells. After differentiation, the characterization of β -cell phenotype was carried out using dithizone and Gomori's staining and further confirmed by mRNA expression study of insulin, Pdx-1, and carbonic anhydrase-9. Insulin production was estimated with ELISA. Aqueous extract of *Tinospora cordifolia* at 15 μ g/ml concentration can effectively induce differentiation of PANC-1 cells into beta cells. The morphological observations

showed brownish-colored dithizone and purple-colored Gomori's staining. The β -cells demonstrated significant mRNA expression of insulin and Pdx-1 and downregulation of carbonic anhydrase-9. The functionality of beta cells was demonstrated by 1.5-fold increase in insulin secretion in response to high glucose. *Tinospora cordifolia* has potential to differentiate PANC-1 ductal cells into functional beta cells and can be a lead towards non-invasive treatment of type 1 diabetes mellitus.

Dawadi P, Syangtan G, Lama B, Kanel SR, Raj Joshi D, Pokhrel LR et al. Understanding COVID-19 Situation in Nepal and Implications for SARS-CoV-2 Transmission and Management. Environ Health Insights. 2022 Jun 7;16:11786302221104348. doi: 10.1177/11786302221104348. eCollection 2022. PMID: 35694428

Abstract:

Background: The pandemic of Coronavirus Disease 2019 (COVID-19), one of the most infectious diseases in the modern history, is caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) and has had a profound health and economic toll, globally. This paper identifies the overall health status associated with COVID-19 pandemic in all 7 provinces of Nepal, a developing country in South Asia, analyzing data from January 2020 to February 2022. It focuses on the SARS-CoV-2 prevalence, transmission through wastewater and other routes, diagnostics, treatment options, and alternative medicines, thereby offering key perspectives for its management.

Materials and methods: Studies regarding coronavirus spanning the 2017 to 2022 period were searched on the web, Nepalese database, and Web of Science. Refined criteria included SARS-CoV-2 in wastewater of Nepal or worldwide. Demographic data (sex, age-group, and geographic location) were also obtained from websites and relevant reports of the Ministry of Health and Population (MOHP) of Nepal, ranging from January 2020 to February 2022. Moreover, trends concerning lockdown, business, and border activities in Nepal between February 2020 and October 2020 were evaluated. The viral dissemination pathways, diagnosis, and available treatment options, including the Ayurvedic medicine, were also examined.

Results: Aerosols generated during the hospital, industrial, recreational, and household activities were found to contribute to the propagation of SARS-CoV-2 into environmental wastewater, thereby putting the surrounding communities at risk of infection. When lockdown ended and businesses opened in October 2020, the number of active cases of COVID-19 increased exponentially. Bagmati Province had the highest number of cases (53.84%), while the remaining 6 provinces tallied 46.16%. Kathmandu district had the highest number of COVID-19 cases (138, 319 cases), while Manang district had the smallest number of infections (81 cases). The male population was found to be predominantly infected (58.7%). The most affected age groups were

the 31 to 40 years old males (25.92%) and the 21 to 30 years old females (26.85%).

Conclusion: The pandemic impacted the public health and economic growth in our study duration. SARS-CoV-2 was prevalent in the wastewater of Nepal. The Terai districts and the megacities were mostly affected by SARS-CoV-2 infections. Working-age groups and males were identified as the highest risk groups. More investigations on the therapeutic and alternative cures are recommended. These findings may guide the researchers and professionals with handling the COVID-19 challenges in developing countries such as Nepal and better prepare for future pandemics.

Deshpande SV, Deshpande VS, Bhosale A, Kadam M. Conservative management of acute prolapsed inter-vertebral disc with ayurveda: A case report. J Ayurveda Integr Med. 2022 Jun 2;13(2):100561. doi: 10.1016/j.jaim.2022.100561. Online ahead of print. PMID: 35661935

Abstract:

Acute prolapsed inter-vertebral disc (IVDP) is a painful condition that requires immediate treatment by conservative or surgical management. Though majority of patients show remission in symptoms with conservative treatment, regression of herniated disc with non-surgical management has been rarely reported. A 46 years old female patient with acute and severe low back pain, disability and radiating pain towards right lower extremity came to our hospital. Oswestry Disability Index (ODI) score of the patient was 94% indicating bed-ridden condition. MRI of lumbar spine showed diffuse posterior disc bulge between fourth and fifth lumbar vertebra indenting right traversing nerve root and inferior displacement of extruded disc along the body of fifth lumbar vertebra. She was treated according to treatment explained in Ayurveda. She received oral medications, application of medicated oils, fomentation and medicated enema (Basti). After treatment of seven and half months, the patient showed good remission in pain, stiffness and radiculopathy. ODI score reduced to 9% that indicates minimal disability. Follow up MRI showed non significant compression of the nerve root and gross reduction in the inferior displacement of extruded disc. Acute IVDP can be successfully conserved using Ayurveda treatment. The Panchakarma procedures and medicines used in the treatment need further evaluation.

Ghezelbash B, Shahrokhi N, Khaksari M, Asadikaram G, Shahrokhi M, Shirazpour S. Protective Roles of Shilajit in Modulating Resistin, Adiponectin, and Cytokines in Rats with Non-alcoholic Fatty Liver Disease. Chin J Integr Med. 2022 Jun;28(6):531-537. doi: 10.1007/s11655-022-3307-3. Epub 2022 Mar 8. PMID: 35258780

Abstract:

Objective: To evaluate the effect of Shilajit, a medicine of Ayurveda, on the serum changes in cytokines and adipokines caused by non-alcoholic fatty liver disease (NAFLD).

Methods: After establishing fatty liver models by feeding a high-fat diet (HFD) for 12 weeks, 35 Wistar male rats were randomly divided into 5 groups, including control (standard diet), Veh (HFD + vehicle), high-dose Shilajit [H-Sh, HFD + 250 mg/(kg·d) Shilajit], low-dose Shilajit [L-Sh, HFD + 150 mg/(kg·d) Shilajit], and pioglitazone [HFD + 10 mg/(kg·d) pioglitazone] groups, 7 rats in each group. After 2-week of gavage administration, serum levels of glucose, insulin, interleukin 1beta (IL-1 β), IL-6, IL-10, tumor necrosis factor-alpha (TNF- α), adiponectin, and resistin were measured, and insulin resistance index (HOMA-IR) was calculated.

Results: After NAFLD induction, the serum level of IL-10 significantly increased and serum IL-1 β , TNF- α levels significantly decreased by injection of both doses of Shilajit and pioglitazone ($P < 0.05$). Increases in serum glucose level and homeostasis model of HOMA-IR were reduced by L-Sh and H-Sh treatment in NAFLD rats ($P < 0.05$). Both doses of Shilajit increased adiponectin and decreased serum resistin levels ($P < 0.05$).

Conclusion: The probable protective role of Shilajit in NAFLD model rats may be via modulating the serum levels of IL-1 β , TNF- α , IL-10, adipokine and resistin, and reducing of HOMA-IR.

Hassanein EHM, Ibrahim IM, Abd-Alhameed EK, Mohamed NM, Ross SA. Protective effects of berberine on various kidney diseases: Emphasis on the promising effects and the underlined molecular mechanisms. Life Sci. 2022 Jun 16:120697. doi: 10.1016/j.lfs.2022.120697. Online ahead of print. PMID: 35718235

Abstract:

Berberine (BBR) is a pentacyclic benzylisoquinoline alkaloid that can be found in diversity of medicinal plants. BBR has a wide range of pharmacological bioactivities, in addition when administrated orally, it has a broad safety margin. It has been used as an antidiarrheal, antimicrobial, and anti-diabetic drug in Ayurvedic and Chinese medicine. Several scholars have found that BBR has promising renoprotective effects against different renal illnesses, including diabetic nephropathy, renal fibrosis, renal ischemia, renal aging, and renal stones. Also, it has renoprotective effects against nephrotoxicity induced by chemotherapy, heavy metal, aminoglycosides, NSAID, and others. These effects imply that BBR has an evolving therapeutic potential against acute renal failure and chronic renal diseases. Hence, we report herein the beneficial therapeutic renoprotective properties of BBR, as well as the highlighted

molecular mechanism. In conclusion, the studies discussed throughout this review will afford a comprehensive overview about renoprotective effect of BBR and its therapeutic impact on different renal diseases.

Jain V, Roy K. Severe Lead Toxicity Due to Ayurvedic Medicine in a Child with Type 1 Diabetes Mellitus: Authors' Reply. Indian J Pediatr. 2022 Jun;89(6):634. doi: 10.1007/s12098-022-04106-2. Epub 2022 Mar 17. PMID: 35298771

Jayakumar T, Kalyani A, Kashyap Bannuru Nanjundaswamy R, Tonni SS. Preliminary Study on the Effect of Bhramari Pranayama on Voice of Prospective Singers. J Voice. 2022 Jun 8:S0892-1997(22)00143-6. doi: 10.1016/j.jvoice.2022.05.010. Online ahead of print. PMID: 35690530

Abstract:

Introduction: Bhramari Pranayama (BP) is a yogic breathing technique that involves producing a vibrating constant pitch sound emulating the buzzing of bumblebee. Since BP deals with breathing and humming in the sustained pitch, it is hypothesized that it can have implications for improving voice quality in individuals. However, there is a dearth of research available to support this assumption. Further, there are no published reports on the effect of BP on voice quality in prospective singers group.

Aim: Current study was taken up to explore the effect induced by BP in the voice characteristics/quality of prospective singers.

Method: The participants included 30 healthy prospective singers in the age range of 18-35 years who were attending music schools within the state of Karnataka, India. BP regimen was demonstrated to all individuals. The voice recordings of the participants were obtained on day 0 and day 30 of BP practice. Acoustic analysis was performed to obtain AVQI and its constituent parameters and voice parameters from the MDVP program.

Result: Among the AVQI and its constituent parameters, Cepstral peak prominence-smoothed, Slope LTAS, and Tilt LTAS showed significant differences before and after BP. MDVP showed a significant difference in tremor measures before and after the practice of BP.

Discussion: Results of the present study indicated positive effects of BP on the voice characteristics of the prospective singers and it is reflected in objective acoustic outcome parameters of AVQI and MDVP. This supports the assumption that BP which involves yogic breathing will have beneficial effects on vocal physiology in turn leading to improved voice quality in these individuals. However, it is of future interest to validate these findings on larger samples and populations with different outcome measures. Also, future

studies are warranted to verify the efficacy of BP in improving vocal quality and vocal efficiency of individuals with dysphonia.

Jiang Z, Guo C, Zhang D. Pressure wrist pulse signal analysis by sparse decomposition using improved Gabor function. *Comput Methods Programs Biomed.* 2022 Jun;219:106766. doi: 10.1016/j.cmpb.2022.106766. Epub 2022 Mar 26. PMID: 35395592

Abstract:

Background and objective: In traditional Chinese medicine and Ayurvedic medicine, wrist pulse wave fluctuations are an important indicator for distinguishing different health states. Owing to the development of modern sensing technology, computational methods have been used in the analysis of pulse wave signals. The description and quantification of the peaks in the pulse wave is significant for the identification of health status.

Methods: In this study, we decomposed the pressure pulse waveform of the radial artery into several components by sparse decomposition with an improved Gabor function. To better represent the position, shape, and relationship of the peaks, we designed an improved Gabor function structure based on the characteristics of the pulse waveform to generate a time-frequency dictionary. Compared with conventional representation methods, the shape of the Gabor function is more variable. In addition, owing to the limitation of windowing, the Gabor function can reduce the influence on other positions when it represents a specific position. Feature vectors consisting of decomposed components can be used for computerized pulse signal analysis and disease diagnosis.

Results: In the binary classification of healthy and diseased pulse signals, the proposed method achieved the best results for health/diabetes, health/cardiac disease, health/hypertension, and health/nephropathy with accuracies of 93.54%, 73.42%, 88.42%, and 82.28%, respectively. The multi-classification performance of the different types of features was evaluated by six classifiers, and the proposed method obtained the highest classification performance with support vector machine-radial basis function for both balanced and imbalanced data.

Conclusions: The results indicated that the proposed method enabled to obtain a smaller representation error and exhibited superior performance in distinguishing between the signals collected from patients and healthy individuals. Moreover, for the multi-classification of the pulse signals, the proposed method performed better than the state-of-the-art methods.

Joshi K, Patwardhan B, Valiathan MS. Ayurvedic Biology and road ahead: The first decade. *J Ayurveda Integr Med.* 2022 Jun 13:100588. doi: 10.1016/j.jaim.2022.100588. Online ahead of print. PMID: 35710895

Kandagalla S, Rimac H, Gurushankar K, Novak J, Grishina M, Potemkin V. Withasomniferol C, a new potential SARS-CoV-2 main protease inhibitor from the Withania somnifera plant proposed by in silico approaches. PeerJ. 2022 Jun 2;10:e13374. doi: 10.7717/peerj.13374. eCollection 2022. PMID: 35673392

Abstract:

Exploring potent herbal medicine candidates is a promising strategy for combating a pandemic in the present global health crisis. In Ayurveda (a traditional medicine system in India), *Withania somnifera* (WS) is one of the most important herbs and it has been used for millennia as Rasayana (a type of juice) for its wide-ranging health benefits. WS phytochemicals display a broad spectrum of biological activities (such as antioxidant, anticancer and antimicrobial) modulate detoxifying enzymes, and enhance immunity. Inspired by the numerous biological actions of WS phytochemicals, the present investigation explored the potential of the WS phytochemicals against the SARS-CoV-2 main protease (3CLpro). We selected 11 specific withanolide compounds, such as withaphysalin, withasomniferol, and withafastuosin, through manual literature curation against 3CLpro. A molecular similarity analysis showed their similarity with compounds that have an established inhibitory activity against the SARS-CoV-2. In silico molecular docking and molecular dynamics simulations elucidated withasomniferol C (WS11) as a potential candidate against SARS-CoV-2 3CLpro. Additionally, the present work also presents a new method of validating docking poses using the AlteQ method.

Khalil HMA, Khalil IA, Al-Mokaddem AK, Hassan M, El-Shiekh RA, Eliwa HA et al. Ashwagandha-loaded nanocapsules improved the behavioral alterations, and blocked MAPK and induced Nrf2 signaling pathways in a hepatic encephalopathy rat model. Drug Deliv Transl Res. 2022 Jun 7. doi: 10.1007/s13346-022-01181-y. Online ahead of print. PMID: 35672652

Abstract:

Ashwagandha (ASH), a vital herb in Ayurvedic medicine, demonstrated potent preclinical hepato- and neuroprotective effects. However, its efficacy is limited due to low oral bioavailability. Accordingly, we encapsulated ASH extract in chitosan-alginate bipolymeric nanocapsules (ASH-BPNCs) to enhance its physical stability and therapeutic effectiveness in the gastrointestinal tract. ASH-BPNC was prepared by emulsification followed by sonication. The NCs showed small particle size (< 220 nm), zeta-potential of 25.2 mV, relatively high entrapment efficiency (79%), physical stability at acidic and neutral pH, and in vitro release profile that extended over 48 h. ASH-BPNC was then investigated in a thioacetamide-induced hepatic encephalopathy (HE) rat

model. Compared with free ASH, ASH-BPNC improved survival, neurological score, general motor activity, and cognitive task-performance. ASH-BPNC restored ALT, AST and ammonia serum levels, and maintained hepatic and brain architecture. ASH-BPNC also restored GSH, MDA, and glutathione synthetase levels, and Nrf2 and MAPK signaling pathways in liver and brain tissues. Moreover, ASH-BPNC downregulated hepatic NF- κ B immunohistochemical expression. Moreover, the in vivo biodistribution studies demonstrated that most of the administered ASH-BPNC is accumulated in the brain and hepatic tissues. In conclusion, chitosan-alginate BPNCs enhanced the hepatoprotective and neuroprotective effects of ASH, thus providing a promising therapeutic approach for HE.

Khandia R, Viswanathan N, Singhal S, Alqahtani T, A Almikhlafi M, Nikolaevich Simonov A et al. Ameliorative effects of phytomedicines on Alzheimer's patients. Curr Alzheimer Res. 2022 Jun 10. doi: 10.2174/1567205019666220610155608. Online ahead of print. PMID: 35692129

Abstract:

Introduction: Alzheimer's Disease (AD) is a progressive, neurodegenerative disease that severely affects affected individuals' cognitive abilities, memory, and quality of life. It affects the elderly population, and there is no permanent prevention or cures available today, treatments mainly aiming to alleviate the symptoms as and when they appear. Alternate therapeutic approaches are being researched constantly, and there is a growing focus on phytomedicine, herbal medicine, organic compounds, ayurvedic compounds for the treatment of AD.

Methods: The current study aims to provide an extensive review of these plants against AD from the currently existing literature. Most relevant keywords like Alzheimer's Disease, phytomedicines, ethnic medicines, the role of phytomedicine in neuroprotection, common phytomedicines against AD etc., were used to select the plants and their metabolites effective in treating AD. The study focuses on six plants: Panax ginseng, Ginkgo biloba, Bacopa monnieri, Withania somnifera, Curcuma longa, and Lavandula angustifolia. Their active components have been studied alongwith, neuroprotective properties, and evidence of in-vitro, pre-clinical studies, and clinical studies conducted to prove their therapeutic potential against the disease have been presented.

Results: All plants envisaged in the study show potential for fighting against AD to varying degrees. Their compounds have shown therapeutic effect by reversing the neurological changes such as clearing A β plaque and neurofibrillary tangle formation, and ameliorative effects against neurodegeneration through processes including improving concentration, memory, cognition and learning, higher working and cue memory, improved

spatial memory, inhibition of NF- κ B expression, inhibiting the release of pro-inflammatory cytokines, inhibition of AChE and lipid peroxidase enzymes, and reduction of interleukin levels and tumor necrosis factor- α .

Conclusion: The present review is a comprehensive and up-to-date analysis supported with the evidentiary proofs from pre-clinical studies, meta-analyses, and review papers related to natural phytochemicals' impact on neurodegenerative disorders like AD.

Kulkarni AV, Hanchanale P, Prakash V, Kalal C, Sharma M, Kumar K et al. *Tinospora Cordifolia (Giloy)-Induced Liver Injury During the COVID-19 Pandemic-Multicenter Nationwide Study From India. Hepatol Commun. 2022 Jun;6(6):1289-1300. doi: 10.1002/hep4.1904. Epub 2022 Feb 6. PMID: 35037744*

Abstract:

Tinospora cordifolia (Giloy) is an herbal supplement commonly used in the Indian alternative medicine system Ayurveda. This herb has been promoted to the public in India as an immune booster to prevent novel coronavirus disease 2019. However, small reports have recently shown an association between Giloy use and the development of herb-induced liver injury (HILI) with autoimmune features in some patients. This large retrospective Indian multicenter study spanning 13 centers at nine locations was designed to identify features and outcomes of HILI temporally associated with Giloy use. Chemical and toxicological analyses of retrieved Giloy samples using state-of-the-art methods were also performed. We report 43 patients, of whom more than half were female, with a median time from initial Giloy consumption to symptom onset of 46 days. Patients presented with acute hepatitis, acute worsening of chronic liver disease (CLD, the most common clinical presentation), or acute liver failure. Causality assessment revealed probable liver injury in 67.4%. The most common autoantibody detected was anti-nuclear antibody. Liver biopsy in a subset revealed HILI associated with autoimmune features and hepatocyte and canalicular cholestasis and neutrophilic and eosinophilic infiltration. Conclusion: Giloy is associated with acute hepatitis with autoimmune features and can unmask autoimmune hepatitis (AIH) in people with silent AIH-related CLD. Further studies on the safety (and efficacy) of untested but heavily promoted herbals in alternative systems of medicine are an unmet need in the interests of public health and are especially important during this global health emergency.

Mitra S, Munni YA, Dash R, Sultana A, Moon IS. Unveiling the effect of *Withania somnifera* on neuronal cytoarchitecture and synaptogenesis: A combined in vitro and network pharmacology approach. Phytother Res. 2022 Jun;36(6):2524-2541. doi: 10.1002/ptr.7466. Epub 2022 Apr 20. PMID: 35443091

Abstract:

Withania somnifera (WS), is known for its remarkable contribution in herbal medicine and Ayurveda, which is therapeutically applied to improve memory and anxiety in patients. However, the pharmacological details of this plant on memory boosting yet remained undefined. This study provides mechanistic insights on the effect of ethanol solution extract of the whole plant of WS (WSEE) on neuritogenesis by combining in vitro and in silico network pharmacology approaches. WSEE promoted significant neuronal growth through early differentiation, axodendritic arborization, and synaptogenesis on primary hippocampal neurons. The network pharmacological study confirmed that the neuritogenic activity is potentially mediated by modulating the neurotrophin signaling pathway, where NRTK1 (TrkA) was revealed as the primary target of WS secondary metabolites. This neurotrophic activity of WSEE was significantly stifled by the presence of TrkA inhibitor, which further confirms the TrkA-dependent activity of WSEE. In addition, a molecular docking study suggested steroidal lactones present in the WS might act as nerve growth factor (NGF)-mimetics, activating TrkA by binding to the NGF-binding domain. As a whole, the findings of the study suggest a significant role of WSEE on neuritogenesis and its potential to function as a therapeutic agent and in drug designing for the prevention and treatment of memory-related neurological disorders.

Nadh AG, Revikumar A, Sudhakaran PR, Nair AS. Identification of potential lead compounds against BACE1 through in-silico screening of phytochemicals of Medhya rasayana plants for Alzheimer's disease management. Comput Biol Med. 2022 Jun;145:105422. doi: 10.1016/j.combiomed.2022.105422. Epub 2022 Mar 24. PMID: 35354103

Abstract:

Alzheimer's disease is a progressive and irreversible neurodegenerative disease that accounts for 70-80% of dementia in the elderly. According to recent clinical data, the incidence of the disease is exponentially increasing with age. Beta-site amyloid precursor protein cleaving enzyme 1 (BACE1) is an important molecule involved in the pathogenesis of Alzheimer's disease due to its early role in the amyloid cascade. Cleavage of amyloid precursor protein by BACE1 is the rate-limiting step leading to the production and aggregation of amyloid-beta plaques. A number of natural products are being identified as non-competitive BACE1 inhibitors. In Ayurveda, Medhya rasayana is a group of medicinal herbs, specifically used for managing neurological disorders and is known to be effective in improving cognition and intellect. This study aimed to analyze the pharmacological activity of bio-active compounds in Medhya rasayana plants against BACE1, employing structure-based docking approach. 11 compounds out of 876 were identified as potential hits, based on docking scores, binding energies, and interactions with the critical residues of

BACE1. Possible neurological activities of these compounds were predicted using PASS server. Out of the 11 compounds screened, two compounds, 'Convolidine' from the plant *Convolvulus pleuricaulis* Choisy and 'N-(4-hydroxybutyl) phthalimide' from *Glycyrrhiza glabra* satisfied the pharmacological parameters of Lipinski rule of filtering and ADMET prediction. The binding stability of these compounds against BACE1 was confirmed by molecular dynamic simulation and post dynamic MM/GBSA calculations. Detailed analysis of the interaction with the critical amino acids in the active site revealed the possible inhibitory potential of these compounds of medicinal plant origin against BACE1.

Nainu F, Salim E, Emran TB, Sharma R. *Drosophila melanogaster* as a Versatile Model for Studying Medically Important Insect Vector-Borne Parasites. *Front Cell Infect Microbiol.* 2022 Jun 2;12:939813. doi: 10.3389/fcimb.2022.939813. eCollection 2022. PMID: 35719344

Naren T, Silkoff D, Forsythe M, Cook J. Case series on treatment of dependence to Kamini Vidrawan Ras with opioid substitution therapy. *Drug Alcohol Rev.* 2022 Jun 16. doi: 10.1111/dar.13505. Online ahead of print. PMID: 35711156

Abstract:

Introduction: A cohort of clients was recognised attending an addiction medicine clinic with similar presentations of opioid dependence from use of a rarely known Ayurvedic medication in a specific ethnic community. This retrospective case series was completed to promote wider recognition and further understanding of dependence on Kamini Vidrawan Ras (Kamini).

Methods: A retrospective file audit of the electronic medical record for clients of an addiction medicine outpatient clinic with a history of dependent use of Kamini identified 12 clients meeting inclusion criteria.

Results: All 12 clients were male, aged 27-41 years, all but one of north Indian origin, predominantly employed and predominantly (but not exclusively) without significant other substance use history. All 12 clients were treated with opioid substitution therapy.

Discussion and conclusions: This case series highlights an opioid dependence syndrome resulting from use of an Ayurvedic medicine by men from a specific area of India, highlighting a potential adverse effect of traditional medicines in ongoing use by migrant and ethnic populations that have emigrated to Australia.

Poornima MS, Sindhu G, Billu A, Sruthi CR, Nisha P, Gogoi P et al. Pretreatment of hydroethanolic extract of *Dillenia indica* L. attenuates oleic acid induced NAFLD in HepG2 cells via modulating SIRT-1/p-LKB-

1/AMPK, HMGCR & PPAR- α signaling pathways. J Ethnopharmacol. 2022 Jun 28;292:115237. doi: 10.1016/j.jep.2022.115237. Epub 2022 Mar 26. PMID: 35351574

Abstract:

Ethnopharmacological relevance: *Dillenia indica* L. is an edible plant from the Dilleniaceae family present in the forest of India and other Asian countries. Different parts of this plant are being used in the traditional system of medicines for various diseases like diabetes, indigestion, asthma, jaundice, and rheumatic pain by various rural communities. This plant is very common among Khamptis traditional healers, the rural community of the Dhemaji district of Assam, ethnic communities of Dibru-Saikhowa Biosphere Reserve of Northeast, India for various medicinal uses. It is observed as a 'vat' suppressant and 'pitta' boosting medicine in Ayurveda.

Aim of the study: The aim of this research was to evaluate the effect of hydroethanolic extract of *Dillenia indica* leaf (DI-HET) against non-alcoholic fatty liver disease (NAFLD) as it is reported effective against jaundice in traditional medicine. We are also planning to see the various molecular mechanisms responsible for its effect if it is efficacious.

Study design/method: An in vitro model for NAFLD was employed in this study. For this HepG2 cells were incubated with 100 μ M of oleic acid (OA) for 24 h. For evaluation of the effect of DI-HET, the extracts (5 or 10 μ g/mL) were pretreated to the OA group. Fenofibrate was the positive control. Various parameters relevant to lipogenesis and β -oxidation of fatty acids like intracellular lipid accumulation, reactive oxygen species (ROS), mitochondrial stress, and key proteins were studied.

Results: DI-HET significantly reduced the intracellular lipid accumulation in OA treated cells. And also substantially decreased the expression of lipogenic proteins and increased β -oxidation in the OA group. OA induced ROS generation was found to reduce with DI-HET treatment. Western blot analysis showed that the expression of LXR- α , SREBP-1C, SREBP-2, HMGCR, FAS, CD-36, and ACOX-1 were downregulated while that of SIRT-1, p-LKB-, p-AMPK, p-ACC, CPT-1, and PPAR- α upregulated in DI-HET treatment. LCMS/MS analysis showed the presence of polyphenols like naringenin, catechin, epicatechin, shikimic acid, syringic acid, vanillic acid, and kaempferol.

Conclusion: These results suggest that DI-HET is effective against NAFLD by activation of the SIRT-1/p-LKB-1/AMPK signaling pathway via polyphenols present in the extract.

Rahman MM, Bibi S, Rahaman MS, Rahman F, Islam F, Khan MS et al. Natural therapeutics and nutraceuticals for lung diseases: Traditional significance, phytochemistry, and pharmacology. Biomed Pharmacother.

2022 Jun;150:113041. doi: 10.1016/j.biopha.2022.113041. Epub 2022 May 6. PMID: 35658211

Abstract:

Background: Lung diseases including chronic obstructive pulmonary disease (COPD), infections like influenza, acute respiratory distress syndrome (ARDS), asthma and pneumonia lung cancer (LC) are common causes of sickness and death worldwide due to their remoteness, cold and harsh climatic conditions, and inaccessible health care facilities.

Purpose: Many drugs have already been proposed for the treatment of lung diseases. Few of them are in clinical trials and have the potential to cure infectious diseases. Plant extracts or herbal products have been extensively used as Traditional Chinese Medicine (TCM) and Indian Ayurveda. Moreover, it has been involved in the inhibition of certain genes/proteins effects to promote regulation of signaling pathways. Natural remedies have been scientifically proven with remarkable bioactivities and are considered a cheap and safe source for lung disease.

Methods: This comprehensive review highlighted the literature about traditional plants and their metabolites with their applications for the treatment of lung diseases through experimental models in humans. Natural drugs information and mode of mechanism have been studied through the literature retrieved by Google Scholar, ScienceDirect, SciFinder, Scopus and Medline PubMed resources against lung diseases.

Results: In vitro, in vivo and computational studies have been explained for natural metabolites derived from plants (like flavonoids, alkaloids, and terpenoids) against different types of lung diseases. Probiotics have also been biologically active therapeutics against cancer, anti-inflammation, antiplatelet, antiviral, and antioxidants associated with lung diseases.

Conclusion: The results of the mentioned natural metabolites repurposed for different lung diseases especially for SARS-CoV-2 should be evaluated more by advance computational applications, experimental models in the biological system, also need to be validated by clinical trials so that we may be able to retrieve potential drugs for most challenging lung diseases especially SARS-CoV-2.

Ratnayake P, Udalamaththa V, Samaratunga U, Seneviratne J, Udagama P. Therapeutic Potential of Skin Stem Cells and Cells of Skin Origin: Effects of Botanical Drugs Derived from Traditional Medicine. Stem Cell Rev Rep. 2022 Jun 1. doi: 10.1007/s12015-022-10388-y. Online ahead of print. PMID: 35648312

Abstract:

Skin, the largest organ of the body, plays a vital role in protecting inner organs. Skin stem cells (SSCs) comprise a group of cells responsible for multiplication and replacement of damaged and non-functional skin cells; thereby help maintain homeostasis of skin functions. SSCs and differentiated cells of the skin such as melanocytes and keratinocytes, have a plethora of applications in regenerative medicine. However, as SSCs reside in small populations in specific niches in the skin, use of external stimulants for cell proliferation in vitro and in vivo is vital. Synthetic and recombinant stimulants though available, pose many challenges due to their exorbitant prices, toxicity issues and side effects. Alternatively, time tested traditional medicine preparations such as polyherbal formulations are widely tested as effective natural stimulants, to mainly stimulate proliferation, and melanogenesis/prevention of melanogenesis of both SSCs and cells of skin origin. Complex, multiple targets, synergistic bioactivities of the phytochemical constituents of herbal preparations amply justify these as natural stimulants. The use of these formulations in clinical applications such as in skin regeneration for burn wounds, wound healing acceleration, enhancement or decrease of melanin pigmentations will be in great demand. Although much multidisciplinary research is being conducted on the use of herbal formulas as stem cell stimulants, very few related clinical trials are yet registered with the NIH clinical trial registry. Therefore, identification/ discovery, in depth investigations culminating in clinical trials, as well as standardization and commercialization of such natural stimulants must be promoted, ensuring the sustainable use of medicinal plants.

Raut A, Dhama-Shah H, Phadke A, Shindikar A, Udipi S, Joshi J et al. Picrorhiza kurroa, Royle ex Benth: Traditional uses, phytopharmacology, and translational potential in therapy of fatty liver disease. J Ayurveda Integr Med. 2022 Jun 1:100558. doi: 10.1016/j.jaim.2022.100558. Online ahead of print. PMID: 35659739

Abstract:

Picrorhiza kurroa Royle ex Benth, Kutki (P.kurroa) is an important medicinal plant, traditionally recommended and used in Ayurveda for millennia, with certain cautions. There has been a significant revival of keen interest in its pharmacology, pharmacognosy, and phytochemistry for the last few decades. The evidence of its hepatoprotective activity, in experimental and clinical studies, accelerated the correlation of the specific phytochemical constituents of P.kurroa with precise pharmacological activities. Iridoid glycosides, particularly picrosides, emerged as the active molecules. For effective translation of traditional remedies into modern therapy, value addition by mechanistic understanding of molecular actions, drug targets, the degrees of efficacy and safety as well as convenient dosage forms is needed. Reverse pharmacology approach and phytopharmaceutical drug category facilitate such a translation. The present review illustrates how a potential translation

of traditional practices of using P.kurroa into a phytochemically standardized, clinically targeted natural product for global unmet medical needs viz. Fatty liver disease can be attained.

Reddy R, Baijnath S, Moodley R, Moodley J, Naicker T, Govender N. South African medicinal plants displaying angiotensin-converting enzyme inhibition: Potential use in the management of preeclampsia. J Ayurveda Integr Med. 2022 Jun 5;13(2):100562. doi: 10.1016/j.jaim.2022.100562. Online ahead of print. PMID: 35675745

Abstract:

In resource-limited settings, such as South Africa, hypertensive disorders of pregnancy such as preeclampsia, is the most common direct cause of maternal deaths. Current management strategies of preeclampsia primarily involve the use of pharmaceutical drugs, which are frequently associated with undesirable side-effects. Moreover, these drugs are often not easily accessible due to financial and economic constraints. Consequently, many patients rely on traditional medicine obtained from medicinal plants to manage health-related conditions. Angiotensin-converting enzyme inhibitors are widely used drugs for the management of preeclampsia. This narrative review aims to highlight the use of indigenous medicinal plants from South Africa with Angiotensin-converting enzyme inhibitory activity whilst also evaluating their potential use in the treatment of hypertension in pregnancy. This information will influence traditional healers and sangomas in their patient management. Furthermore, the antihypertensive potential of these plants will be unraveled thus facilitating the development of new naturally occurring pharmaceutical products to reduce maternal and neonatal mortality and morbidity.

Sasidhar V, Puthiyedath R, Lal A. Effectiveness of Mathulungadi Nasyam in the prophylaxis of COVID19 infection - Retrospective analysis of Clinical Data. J Ayurveda Integr Med. 2022 Jun 7:100600. doi: 10.1016/j.jaim.2022.100600. Online ahead of print. PMID: 35693194

Shah SB, Guttal GK, Chikkanna U, Sajjanar NJ. Efficacy of Pippali in vardhamana and fixed dosage pattern in primary hypothyroidism - A randomized clinical trial. J Ayurveda Integr Med. 2022 Jun 2;13(2):100555. doi: 10.1016/j.jaim.2022.100555. Online ahead of print. PMID: 35661936

Abstract:

Introduction: Hypothyroidism is an endocrine condition. The signs and symptoms of Hypothyroidism match with the descriptions of several conditions like Vataja Shotha, Rasa Pradoshaja Vikara or a disorder Agni. In the current study two different dosage forms i.e., Vardhamana (Increasing & Decreasing pattern) and fixed Dosage to evaluate its efficacy on Primary Hypothyroidism.

Materials and methods: 40 patients randomized into two groups Escalating and Fixed were administered Vardhamana Pippali in two dosage forms for 19 days. Serum T3, T4, and TSH were assessed at baseline and on the 20th day along with the assessment of clinical score through Zulewskis's clinical score for measuring tissue hypothyroidism. The total pippali administered in both groups was 69 g.

Results: The mean levels of TSH were 9.52 ± 3.97 mIU/ml, 10 ± 6.02 mIU/ml, and 10.21 ± 8.49 mIU/ml at baseline, 20th day and 40th day respectively in group A. In group B it was 9.21 ± 3.72 mIU/ml, 8.23 ± 4.62 mIU/ml, and 9.15 ± 4.67 mIU/ml at baseline, 20th day and 40th day respectively. The mean Zulewski's clinical score was 3.67 ± 1.49 , 2.28 ± 1.32 , and 2.06 ± 1.25 at baseline, 20th day, and 40th day respectively in Escalating group. In Fixed group it was 3.83 ± 1.20 , 2.50 ± 1.42 , and 3.44 ± 1.33 at baseline, 20th day, and 40th day respectively.

Discussion: Zulewski's clinical scores were statically non-significant in both the groups on the 20th-day respectively, suggesting minimal efficacy of the interventions. But subjects administered with Vardhamana Pippali exhibited better long-lasting effects suggesting sustained effects of the drug.

Conclusion: Pippali is efficacious in reducing the signs and symptoms of Primary Hypothyroidism and also has a positive impact on the Thyroid profile but is more effective when administered in Vardhamana dosage compared to fixed dose.

Siddhu NSS, Guru A, Satish Kumar RC, Almutairi BO, Almutairi MH, Juliet A et al. Pro-inflammatory cytokine molecules from *Boswellia serrate* suppresses lipopolysaccharides induced inflammation demonstrated in an in-vivo zebrafish larval model. Mol Biol Rep. 2022 Jun 18. doi: 10.1007/s11033-022-07544-5. Online ahead of print. PMID: 35716287

Abstract:

Background: *Boswellia serrate* is an ancient and highly valued ayurvedic herb. Its extracts have been used in medicine for centuries to treat a wide variety of chronic inflammatory diseases. However, the mechanism by which *B. serrata* hydro alcoholic extract inhibited pro-inflammatory cytokines in zebrafish (*Danio rerio*) larvae with LPS-induced inflammation remained unknown.

Methods: LC-MS analysis was used to investigate the extract's phytochemical components. To determine the toxicity of *B. serrata* extract, cytotoxicity and embryo toxicity tests were performed. The in-vivo zebrafish larvae model was used to evaluate the antioxidant and anti-inflammatory activity of *B. serrata* extract.

Results: According to an in silico study using molecular docking and ADMET, the compounds acetyl-11-keto-boswellic and 11-keto-beta-boswellic acid present in the extract had higher binding affinity for the inflammatory specific receptor, and it is predicted to be an orally active molecule. In both in-vitro L6 cells and in-vivo zebrafish larvae, 160 µg/mL concentration of extract caused a high rate of lethality. The extract was found to have a protective effect against LPS-induced inflammation at concentrations ranged between 10 and 80 µg/mL. In zebrafish larvae, 80 µg/mL of treatment significantly lowered the level of intracellular ROS, apoptosis, lipid peroxidation, and nitric oxide. Similarly, zebrafish larvae treated with *B. serrata* extract (80 µg/mL) showed an increased anti-inflammatory activity by lowering inflammatory specific gene expression (iNOS, TNF-α, COX-2, and IL-1).

Conclusions: Overall, our findings suggest that *B. serrata* can act as a potent redox scavenger against LPS-induced inflammation in zebrafish larvae and an inhibitor of specific inflammatory genes.

Singh H, Srivastava S, Yadav B, Rai AK, Jameela S, Muralidharan S et al. AYUSH-64 as an adjunct to standard care in mild to moderate COVID-19: An open-label randomized controlled trial in Chandigarh, India. Complement Ther Med. 2022 Jun;66:102814. doi: 10.1016/j.ctim.2022.102814. Epub 2022 Feb 8. PMID: 35149205

Abstract:

Objective: To determine the therapeutic efficacy and safety of AYUSH-64 as an add-on to standard care in mild to moderate COVID-19.

Design setting, and interventions: This open-label randomized controlled parallel-group trial was conducted at a designated COVID care centre in India in 80 patients diagnosed with mild to moderate COVID-19 and randomized into two groups. Participants in the AYUSH-64 add-on group (AG) received AYUSH-64 two tablets (500 mg each) three times a day for 30 days along with standard conventional care. The control group (CG) received standard care alone.

Main outcome measures: Proportion of participants who attained clinical recovery on day 7, 15, 23 and 30, proportion of participants with negative RT-PCR assay for COVID-19 at each weekly time point, change in pro-inflammatory markers, metabolic functions, HRCT chest (CO-RADS category) and incidence of Adverse Drug Reaction (ADR)/Adverse Event (AE).

Results: Out of 80 participants, 74 (37 in each group) contributed to the final analysis. Significant difference was observed in clinical recovery in the AG ($p < 0.001$) compared to CG. Mean duration for clinical recovery in AG (5.8 ± 2.67 days) was significantly less compared to CG (10.0 ± 4.06 days). Significant

improvement in HRCT chest was observed in AG ($p = 0.031$) unlike in CG ($p = 0.210$). No ADR/SAE was observed or reported in AG.

Conclusions: AYUSH-64 as adjunct to standard care is safe and effective in hastening clinical recovery in mild to moderate COVID-19. The efficacy may be further validated by larger multi-center double-blind trials.

Varghese T, Vijayakumar S, Boban N, R SS, L V, Robin DT et al. Severe Lead Toxicity Due to Ayurvedic Medicine in a Child with Type 1 Diabetes Mellitus: Correspondence. Indian J Pediatr. 2022 Jun;89(6):633. doi: 10.1007/s12098-022-04088-1. Epub 2022 Feb 16. PMID: 35171435

Yarazari SB, Jayaraj M. GC-MS Analysis of Bioactive Compounds of Flower Extracts of *Calycopteris floribunda* Lam.: A Multi Potent Medicinal Plant. Appl Biochem Biotechnol. 2022 Jun 11. doi: 10.1007/s12010-022-03993-7. Online ahead of print. PMID: 35689756

Abstract:

Calycopteris floribunda Lam. is a potent medicinal woody climber that belongs to Combretaceae. This plant is usually found in dry deciduous tropical forests and is used in various medicinal practices like Ayurveda, Unani and Sidda. Whole plant and its different parts like leaves, flowers and stem are used in the treatment of diarrhoea, dysentery, jaundice and malaria. It is also have anthelmintic, anti-inflammatory, antifungal, hepatoprotective and anticancerous activities. Knowing its medicinal properties, the present study is undertaken to investigate the preliminary phytochemical constituents and bioactive compounds of flower extracts by GC-MS. GC-MS analysis of flower extracts revealed the presence of over all 41 compounds, of which, acetone and ethanol extracts showed the presence of 13 compounds each, chloroform extract 8 and petroleum ether extract 7 compounds. Some compounds were common in two and three extracts only. The significant bioactive compounds identified are 1,2-benzenedicarboxylic acid (59.81%) in chloroform extract, triterpene lupeol (34.98%) in ethanol extract, tetratetracontane (26.99%) in petroleum ether extract and gamma sitosterol (22.04%) in acetone extract.

UNANI MEDICINE

Ahmad W, Sofi G, Alam MA, Zulkifle M, Ahmad B. Understanding Holism in the light of principle underlying practice of Unani Medicine. Rev Environ Health. 2021 May 13;37(2):189-199. doi: 10.1515/reveh-2021-0009. Print 2022 Jun 27. PMID: 33984879

Abstract:

The holistic Unani medicine is fundamentally different from the reductionist conventional medicine. It asserts the self-integration amongst its basic disciplines, without considering them underlying principles of Unani system of medicine cannot be understood. The diagnosis, selection of drugs, and plan of treatment is also overlooked. Unani scholars attribute health to the functions or actions of the body in a normal way. The constitution is considered as the result of need based on the amalgamation of Arkan (primordial essence). Umoor Tabiya (basic principles) interact at many levels and manifest into Kaifiyyat (Mizaj), Akhlat (Humour), Arwaah (Pneuma), Quwa (faculties), and Tabiyat (Physis) which need to be understood properly for effective management and diagnosis of disease in Unani medicine as well as its treatment. Ilmul Asbab is applied in the prevention of disease as well as in disease causation. In Unani medicine, there should be conformity in between, Asbab (causes), Alamaat (symptoms), and therapeutics. Therefore; the treatment strategy needs the knowledge of Ilmul Asbab. This paper will examine the basic relationship amongst disciplines i.e. Basic principles, diagnosis, and principles of treatment. It will attempt to illustrate the need for awareness of the basic principles of health and disease for a physician for effective management of disease which is what Unani medicine claims to be holistic.

Khatoon F, Azahar M, Jabeen A, Uddin Q, Husain N, Rasheed Naikodi MA. Treatment of chronic plaque psoriasis with herbal unani formulations: A randomized control trial of efficacy and safety. J Ethnopharmacol. 2022 Jun 17:115456. doi: 10.1016/j.jep.2022.115456. Online ahead of print. PMID: 35724745

Abstract:

Ethnopharmacological relevancePsoriasis, despite modern therapeutic options, is incurable and recurrent. In Unani (Greco-Arab) medicine, many medications and formulations have been prescribed by eminent scholars for conditions clinically similar to psoriasis, though empirical evidence is sparse. Hence, the experimental formulations ItrifalShāhtra and MarhamḤina were chosen to be compared to the standard therapies PUVAsol and petrolatum for their safety and efficacy.

Materials and methods: This open-label, randomized control clinical trial was conducted on 66 male and female participants with chronic plaque psoriasis, ranging in age from 18 to 65 years. In each group, 33 participants were block randomized to either receive test formulations or control drugs for 12 weeks. The Unani group received oral Itrīfal Shāhtra (a semisolid paste) and topical MarhamḤina (an ointment) twice daily, and the control group received oral 8-methoxypsoralen and topical petroleum jelly for local application. Participants of both groups were advised to get daily sunlight exposure for 5-15 min. The primary outcome measure was the change in psoriasis area and severity index (PASI) assessed at each visit. Secondary outcome measures were patient global assessment on a 100 mm VAS applied at baseline and after 12 weeks of treatment and change in subjective parameters including erythema, induration, scaling, and itching, assessed on a 5-point scale at every visit. Hemogram, LFTs, RFTs, CXR, ECG, urine, and stool tests were all assessed at baseline and after treatment for the safety of the drugs.

Results: The per-protocol analysis was done on 25 participants in each group. The mean \pm SD of the psoriasis area severity index (PASI) significantly decreased from 27.88 ± 12.01 and 23.61 ± 9.79 at baseline to 5.01 ± 4.59 and 9.85 ± 7.16 after completion of the trial therapies in both Unani and control groups, respectively. Also, the test formulations outperformed the control drugs on clinically significant endpoints, PASI 50 and PASI 75, with all 25 participants achieving PASI 50 and 76% achieving PASI 75.

Conclusion: The trial formulations, ItrīfalShāhtraand MarhamḤinamay be superior to control drugs PUVAsol and petrolatum in terms of safety, efficacy, and tolerability in the treatment of chronic plaque psoriasis. Thus, the Unani formulations may further be evaluated in a well-designed multicentric superiority trial with an adequate sample size.

Mahfooz S, Itrat M, Uddin H, Khan TN. Unani medicinal herbs as potential air disinfectants: an evidence-based review. Rev Environ Health. 2021 Aug 12;37(2):155-168. doi: 10.1515/reveh-2021-0087. Print 2022 Jun 27. PMID: 34384009

Abstract:

Objectives: Indoor air quality has a significant impact on our health and quality of life, as people spends 80-90% of their time indoors. Fumigation of several medicinal herbs has been recommended by Unani scholars to improve air quality, but their efficacy in air purification is still unknown. Hence, this article aims to discuss the applicability of proposed medicinal herbs in the light of current researches.

Methods: A manual literature survey of classical Unani texts was conducted to collect information about the herbs recommended for air purification. In

addition, research databases such as PubMed, Google Scholar, and ScienceDirect were extensively searched for evidence on the efficacy and mechanism of action of the suggested herbs in air purification.

Results: In classical Unani texts, authors have found descriptions of 26 herbs that have been recommended for improving air quality. In-vitro studies have confirmed the antimicrobial activity of 19 of these herbs. Moreover, the efficacy of *Styrax benzoin*, *Commiphora myrrha* and *Acorus calamus* fumigation on aerial microbes have also been validated by studies.

Conclusions: The findings of the literature review clearly demonstrated that the herbs recommended by Unani scholars for air purification have broad-spectrum antimicrobial activity, indicating that these herbs could be a potential candidate for air disinfectant. Therefore, authors recommend the further researches on proposed herbs to validate their efficiency against airborne pathogens in the vapour phase.

SIDDHA

Shanmugam K, Nirmala A, Parthiban P, Pitchiah Kumar M, Dhanam C, Ganesh S et al. Safety and Efficacy of Siddha Medicine preparation in the management of COVID-19: A Prospective Randomised Open Label Study. J Ayurveda Integr Med. 2022 Jun 3:100597. doi: 10.1016/j.jaim.2022.100597. Online ahead of print. PMID: 35677618

Abstract:

Background: The use of complementary and alternative medicine (CAM) therapies has surged since the spread of COVID-19 pandemic. However, the efficacy and safety of these CAM therapies remains majorly unexplored. Objective of the current study is to understand the efficacy and safety of one such traditional CAM therapy of South India, known as 'Siddha' system of medicine, in the management for the COVID-19 patients.

Methods: We conducted a randomised, controlled, open label trial in patients hospitalized with SARS-CoV-2 infection who had an oxygen saturation of 90% or more while breathing ambient air. Patients were randomized into two groups in a 1:1 ratio to either intervention group, receiving seven days of siddha medicine (Intervention group; n=50) or standard care (control group; n=50). The primary end point was clinical markers and patient recovery status on day 8.

Results: A total of 100 patients with confirmed COVID-19 with average age of 37 yrs (interquartile range, 28-49) participated in the study. There was no statistically difference between groups at baseline ($P>0.05$). After intervention, patients in the intervention group had statistically ($P<0.05$) significant reduction in the symptoms when compared to standard care. By end of the intervention period, 6 patients (12%) were hospitalized in the control group and none of them were reported for intervention group.

Conclusion: Among patients with mild to moderate COVID-19, 7 days of siddha medicine showed a significant reduction in the clinical symptoms and requirement of hospitalisation, with no adverse events. Therefore, the particular siddha medicine preparation could be used safely and effectively for the management of COVID-19 patients.

YOGA

Dos Santos GM, Verlengia R, Ribeiro AGSV, Corrêa CA, Ciuldim M, Crisp AH. Yoga and mental health among Brazilian practitioners during COVID-19: An internet-based cross-sectional survey. Sports Med Health Sci. 2022 Jun;4(2):127-132. doi: 10.1016/j.smhs.2022.04.005. Epub 2022 May 7. PMID: 35574287

Abstract:

This study aimed to describe yoga practice and verify its association with depression, anxiety, and stress during the COVID-19 pandemic among Brazilian practitioners. A cross-sectional anonymous online survey was conducted in all regions of Brazil using a snowball sampling strategy among yoga practitioners. A total of 860 participants (87% female, aged: 19-82 years) completed the survey. Sociodemographic data, lifestyle factors, yoga practice during the pandemic, and the Depression Anxiety and Stress Scale (DASS-21) scores were collected between July 9 and July 15, 2021. Overall, 9.5%, 9.3%, and 5.6% of participants exhibited some traits (mild to severe) of depression, anxiety, and stress, respectively. Hatha yoga (48%) was the most commonly practiced yoga style. In the adjusted analysis, a higher yoga experience (> 5 years) was associated with better anxiety (odds ratio; bootstrap 95% confidence interval: 2.42; 1.32, 4.49) and stress status (1.80; 1.06, 3.00) than beginners (< 1 year). Practitioners who reported higher time and days of yoga practice during the study period were more likely to show normal levels of depression (odds ratio: 2.56-6.49; $p < 0.05$), anxiety (odds ratio: 3.68-8.84; $p < 0.05$), and stress (odds ratio: 2.15-5.21; $p < 0.05$). Moreover, the maintenance of practice frequency during the pandemic was associated with higher odds of normal levels of depression (2.27; 1.39-3.79), anxiety (1.97; 1.25-3.10), and stress (1.97; 1.32-2.96). In conclusion, our findings indicated that a higher level of yoga practice was associated with better mental health levels during the COVID-19 pandemic.

Guest E, Zucchelli F, Costa B, Bhatia R, Halliwell E, Harcourt D. Systematic review of interventions aiming to promote positive body image in children and adolescents. Body Image. 2022 Jun 6;42:58-74. doi: 10.1016/j.bodyim.2022.04.009. Online ahead of print. PMID: 35679652

Abstract:

Evidence shows interventions can improve positive body image in adult women. This systematic review examined the evidence of efficacy of interventions that aimed to increase positive body image in children and young people aged under 18 years. The authors followed PRISMA guidelines for the review. Searches of CINAHL Plus, Medline, PsychINFO, Wiley Online Library, SCOPUS and grey literature were conducted up to February 2021 and

identified 4171 papers. Thirteen studies evaluating 12 interventions, designed for children/adolescents aged 9-18 years, were eligible and evaluated using the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool. The studies evaluated body appreciation, body-esteem, and embodiment. Studies using cognitive dissonance, peer support, and psychoeducation had evidence of improving body appreciation and body-esteem in adolescent girls. However, evidence of efficacy for younger children and boys was lacking and the studies ranged in methodological quality. Further research should rigorously evaluate positive body image interventions using second-generation measures that assess specific components of positive body image and consider how to promote positive body image in young children and boys.

Hazzard VM, Burnette CB, Hooper L, Larson N, Eisenberg ME, Neumark-Sztainer D. Lifestyle health behavior correlates of intuitive eating in a population-based sample of men and women. *Eat Behav.* 2022 Jun 6;46:101644. doi: 10.1016/j.eatbeh.2022.101644. Online ahead of print. PMID: 35691254

Abstract:

The aim of this observational study was to examine how lifestyle health behaviors hypothesized to influence attunement to internal cues (breakfast consumption frequency, physical activity, yoga practice, sleep, and recreational screen time) are cross-sectionally related to intuitive eating (IE). Data from 765 men and 1009 women ($M_{age} = 31.1 \pm 1.7$ years) who participated in Project EAT-IV (Eating and Activity in Teens and Young Adults) were analyzed with sex-stratified linear regression models adjusted for age, race/ethnicity, socioeconomic background, and parent status. Sociodemographic-adjusted mean levels of each health behavior by sex were generated at low (one standard deviation below the mean), average (at the mean), and high (one standard deviation above the mean) levels of IE to facilitate interpretation of regression results. Among women only, more frequent breakfast consumption ($p = .02$), more time spent practicing yoga ($p = .03$), more sleep ($p = .004$), and less recreational screen time ($p = .01$) were each significantly associated with higher IE after adjusting for sociodemographic characteristics. Compared to women with low IE, women with high IE reported, on average, eating breakfast 0.3 more days a week, practicing 12 more minutes of yoga per week, getting 12 more minutes of sleep per night, and engaging in 18 fewer minutes of recreational screen time per day. Results suggest that these modifiable health behaviors may be valuable targets for interventions to increase IE among women, though longitudinal research is needed to elucidate the temporality of these associations.

Jagadeesan T, R A, R K, Jain T, Allu AR, Selvi G T et al. Effect of Bhramari Pranayama intervention on stress, anxiety, depression and sleep quality among COVID 19 patients in home isolation. *J Ayurveda Integr Med.* 2022

Jun 6:100596. doi: 10.1016/j.jaim.2022.100596. Online ahead of print. PMID: 35693195

Abstract:

Background: COVID-19 outbreak is considered to be a major public health concern as it has a negative impact on the patient's psychological health. In addition, patients under home isolation might be more panic and in stress. In this study, we examined the effect of Bhramari Pranayama (Bhr.P) intervention on patients' psychological distress during home isolation.

Methods: Ninety-two asymptomatic COVID-19 patients were recruited from the host hospital and willing patients who satisfied the inclusion criteria (n=42) were selected for the study. The patients were given Bhr.P intervention (20 min) through online for 15 days. Participants were assessed with Depression Anxiety and Stress Scale-21(DASS-21), Pittsburgh Sleep Quality Index (PSQI), and Quality of life (WHOQOL-BREF) at baseline and post-intervention.

Results: Bhr.P practice has shown a significant ($P<0.05$) reduction in DASS-21 score of depression, anxiety and stress. In addition, the patients stated significant improvement in quality of sleep (PSQI; $p<0.05$) and quality of life (WHOQOL-BREF; $p<0.05$) after the intervention.

Conclusion: Our findings indicate that Bhr.P intervention had a positive impact on psychological health as well as quality of sleep among the COVID-19 patients during home isolation. However, it needs to be confirmed by multi-site randomized controlled trials.

James Palmer A, Anderson EZ, Daneault JF. Remote Delivery of Yoga Interventions Through Technology: Scoping Review. J Med Internet Res. 2022 Jun 6;24(6):e29092. doi: 10.2196/29092. PMID: 35666562

Abstract:

Background: The popularity of yoga and the understanding of its potential health benefits have recently increased. Unfortunately, not everyone can easily engage in in-person yoga classes. Over the past decade, the use of remotely delivered yoga has increased in real-world applications. However, the state of the related scientific literature is unclear.

Objective: This scoping review aimed to identify gaps in the literature related to the remote delivery of yoga interventions, including gaps related to the populations studied, the yoga intervention characteristics (delivery methods and intervention components implemented), the safety and feasibility of the interventions, and the preliminary efficacy of the interventions.

Methods: This scoping review was conducted in accordance with the PRISMA-ScR (Preferred Reporting Item for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) guidelines. Scientific databases were searched throughout April 2021 for experimental studies involving yoga delivered through technology. Eligibility was assessed through abstract and title screening and a subsequent full-article review. The included articles were appraised for quality, and data were extracted from each article.

Results: A total of 12 studies of weak to moderate quality were included. Populations varied in physical and mental health status. Of the 12 studies, 10 (83%) implemented asynchronous delivery methods (via prerecorded material), 1 (8%) implemented synchronous delivery methods (through videoconferencing), and 1 (8%) did not clearly describe the delivery method. Yoga interventions were heterogeneous in style and prescribed dose but primarily included yoga intervention components of postures, breathing, and relaxation and meditation. Owing to the heterogeneous nature of the included studies, conclusive findings regarding the preliminary efficacy of the interventions could not be ascertained.

Conclusions: Several gaps in the literature were identified. Overall, this review showed that more attention needs to be paid to yoga intervention delivery methods while designing studies and developing interventions. Decisions regarding delivery methods should be justified and not made arbitrarily. Studies of high methodological rigor and robust reporting are needed.

Krejci M, Hill M, Kajzar J, Tichy M, Hosek V. Yoga Exercise Intervention Improves Balance Control and Prevents Falls in Seniors Aged 65. Zdr Varst. 2022 Mar 21;61(2):85-92. doi: 10.2478/sjph-2022-0012. eCollection 2022 Jun. PMID: 35432608

Abstract:

Introduction: Body balance control represents a key factor preventing falls and subsequent injuries in seniors aged 65+. Intervention based on yoga exercises seem to be effective in improving balance.

Objective: The objective is to analyse and compare changes in static, dynamic, and total balance scores, changes in body composition and social indices as effects of yoga-based intervention.

Methods: A total of 500 participants (234 men aged 74.5 SD±7.74 and 266 women aged 76.9 SD±7.23) were assessed using the Tinetti Balance Assessment Tool, the InBody 230 bioimpedance body composition analyser, and the SF-36 Health Survey, applied to pre and post-testing. The experimental group (n=262; 122 males; 140 females) underwent a four-week yoga-based intervention, 30 minutes daily, while the control group (n=238; 112 males; 126 females) underwent its usual daily programme at senior homes or

centres. The ANOVA model, consisting of the Group, Stage, Subject and Group × Stage interaction factors, was used for data evaluation.

Results: Intervention led to improvements in the static, dynamic and total balance scores in the experimental group compared to the control group. The results of SF-36 showed positive changes in the psychosocial aspects of health, such as promoting of calmness and happiness in male seniors and reducing fatigue, nervousness and depression in female seniors. The post-intervention decrease in body fat percentage and increase in muscle mass in seniors is discussed.

Conclusions: The four-week yoga-based intervention had positive effects on the static, dynamic and total balance scores, body composition and social status.

Krese KA, Donnelly KZ, Etingen B, Bender Pape TL, Chaudhuri S, Aaronson AL et al. Feasibility of a Combined Neuromodulation and Yoga Intervention for Mild Traumatic Brain Injury and Chronic Pain: Protocol for an Open-label Pilot Trial. JMIR Res Protoc. 2022 Jun 15;11(6):e37836. doi: 10.2196/37836. PMID: 35704372

Abstract:

Background: Mild traumatic brain injury (mTBI) and chronic pain often co-occur and worsen rehabilitation outcomes. There is a need for improved multimodal nonpharmacologic treatments that could improve outcomes for both conditions. Yoga is a promising activity-based intervention for mTBI and chronic pain, and neuromodulation through transcranial magnetic stimulation is a promising noninvasive, nonpharmacological treatment for mTBI and chronic pain. Intermittent theta burst stimulation (iTBS) is a type of patterned, excitatory transcranial magnetic stimulation. iTBS can induce a window of neuroplasticity, making it ideally suited to boost the effects of treatments provided after it. Thus, iTBS may magnify the impacts of subsequently delivered interventions as compared to delivering those interventions alone and accordingly boost their impact on outcomes.

Objective: The aim of this study is to (1) develop a combined iTBS+yoga intervention for mTBI and chronic pain, (2) assess the intervention's feasibility and acceptability, and (3) gather preliminary clinical outcome data on quality of life, function, and pain that will guide future studies.

Methods: This is a mixed methods, pilot, open-labeled, within-subject intervention study. We will enroll 20 US military veteran participants. The combined iTBS+yoga intervention will be provided in small group settings once a week for 6 weeks. The yoga intervention will follow the LoveYourBrain yoga protocol-specifically developed for individuals with TBI. iTBS will be administered immediately prior to the LoveYourBrain yoga session. We will

collect preliminary quantitative outcome data before and after the intervention related to quality of life (TBI-quality of life), function (Mayo-Portland Adaptability Index), and pain (Brief Pain Inventory) to inform larger studies. We will collect qualitative data via semistructured interviews focused on intervention acceptability after completion of the intervention.

Results: This study protocol was approved by Edward Hines Jr Veterans Administration Hospital Institutional Review Board (Hines IRB 1573116-4) and was prospectively registered on ClinicalTrials.gov (NCT04517604). This study includes a Food and Drug Administration Investigational Device Exemption (IDE: G200195). A 2-year research plan timeline was developed. As of March 2022, a total of 6 veterans have enrolled in the study. Data collection is ongoing and will be completed by November 2022. We expect the results of this study to be available by October 2024.

Conclusions: We will be able to provide preliminary evidence of safety, feasibility, and acceptability of a novel combined iTBS and yoga intervention for mTBI and chronic pain-conditions with unmet treatment needs.

Leach HJ, Hidde MC, Portz JD, Van Puymbroeck M, Sharp JL, Fox AL et al. Matching Exercise Volume in Active Control Groups for Yoga Interventions. *Altern Ther Health Med.* 2022 Jun 10:AT7433. Online ahead of print. PMID: 35687710

Abstract:

Context: The selection of a control group should foremost be determined by the study's primary intended outcome and trial design. When examining the effects of the physical movements that comprise yoga postures, an active control group, with physical exercise as the control, is often recommended.

Objective: The current study aimed to define an active control group that participates in physical exercise, emphasizing the importance of matching the exercise's volume to that of an intervention group's yoga, and to provide a tangible example from a federally funded, recently completed, randomized controlled trial.

Design: The research team designed a control group, providing a case study as an example of it.

Setting: The study took place at Colorado State University.

Intervention: The exercise component for the control group included 60 minutes of low-intensity exercise, matched with 60 minutes of Hatha yoga for the intervention group. Because the intervention included chronic pain self-management in addition to the exercise component, the education component

for the control group included 45 minutes of group-based, general health-and-wellness education and discussion.

Conclusions: Future randomized trials for yoga and other complementary or integrative health interventions should continue to use appropriate active control groups, which will serve to enhance the scientific rigor of conclusions that can be drawn with respect to the effectiveness of these interventions.

Munoz-Vergara D, Grabowska W, Yeh GY, Khalsa SB, Schreiber KL, Huang CA et al. Systematic review of in vivo stretching regimens on inflammation and its relevance to translational yoga research. PLoS One. 2022 Jun 1;17(6):e0269300. doi: 10.1371/journal.pone.0269300. eCollection 2022. PMID: 35648793

Abstract:

Objective: To conduct a systematic review evaluating the impact of stretching on inflammation and its resolution using in vivo rodent models. Findings are evaluated for their potential to inform the design of clinical yoga studies to assess the impact of yogic stretching on inflammation and health.

Methods: Studies were identified using four databases. Eligible publications included English original peer-reviewed articles between 1900-May 2020. Studies included those investigating the effect of different stretching techniques administered to a whole rodent model and evaluating at least one inflammatory outcome. Studies stretching the musculoskeletal and integumentary systems were considered. Two reviewers removed duplicates, screened abstracts, conducted full-text reviews, and assessed methodological quality.

Results: Of 766 studies identified, 25 were included for synthesis. Seven (28%) studies had a high risk of bias in 3 out of 10 criteria. Experimental stretching protocols resulted in a continuum of inflammatory responses with therapeutic and injurious effects, which varied with a combination of three stretching parameters--duration, frequency, and intensity. Relative to injurious stretching, therapeutic stretching featured longer-term stretching protocols. Evidence of pro- and mixed-inflammatory effects of stretching was found in 16 muscle studies. Evidence of pro-, anti-, and mixed-inflammatory effects was found in nine longer-term stretching studies of the integumentary system.

Conclusion: Despite the overall high quality of these summarized studies, evaluation of stretching protocols paralleling yogic stretching is limited. Both injurious and therapeutic stretching induce aspects of inflammatory responses that varied among the different stretching protocols. Inflammatory markers, such as cytokines, are potential outcomes to consider in clinical yoga studies. Future translational research evaluating therapeutic benefits should consider in vitro studies, active vs. passive stretching, shorter-term vs. longer-term

interventions, systemic vs. local effects of stretching, animal models resembling human anatomy, control and estimation of non-specific stresses, development of in vivo self-stretching paradigms targeting myofascial tissues, and in vivo models accounting for gross musculoskeletal posture.

Oka T, Lkhagvasuren B. Effects of practicing yoga on alexisomia: an open-label trial. *Biopsychosoc Med.* 2022 Jun 3;16(1):14. doi: 10.1186/s13030-022-00243-4. PMID: 35659341

Abstract:

Background: Alexisomia refers to difficulties in the awareness and expression of somatic feelings. This idea was proposed by Dr. Yujiro Ikemi as a characteristic observed in patients with psychosomatic diseases and is based on his observations that patients with psychosomatic diseases have difficulty in the awareness and expression of not only their emotions, i.e., alexithymia, but also somatic feelings and sensations, i.e., alexisomia. He also proposed that treating alexisomia is important in the treatment of psychosomatic diseases and that yoga might help improve alexisomia. However, no study has investigated if yoga actually affects alexisomia. This open-label pilot study investigated whether practicing yoga in a class results in change in patients with alexisomia and alexithymia.

Methods: The Shitsu-taikan-sho Scale (STSS) and the Toronto Alexithymia Scale (TAS-20) were administered to 305 participants, including 64 healthy participants, 111 participants who had subjective symptoms without abnormal findings, and 130 participants with chronic diseases. Participants were tested before and 3 months after attending yoga classes.

Results: Yoga practice reduced the STSS and the TAS-20 difficulty in identifying feelings (DIF) subscale scores. Multiple linear regression indicated that a reduction in the TAS-20 DIF subscale scores predicted a decrease in the STSS score, whereas reductions in the STSS difficulty in identifying bodily feelings (DIB) and the lack of health management based on bodily feelings (LHM) subscale scores predicted a decrease in the TAS-20 scores.

Conclusion: We found that regular yoga practice improves alexisomia. Yoga-induced improvement of alexisomia may be mediated, at least in part, by an improvement of DIF in alexithymia. Yoga would be a promising therapeutic approach to improve alexisomia.

O'Shea M, Capon H, Skvarc D, Evans S, McIver S, Harris J et al. Pragmatic preference trial of therapeutic yoga as an adjunct to group cognitive behaviour therapy versus group CBT alone for depression and anxiety. *J Affect Disord.* 2022 Jun 15;307:1-10. doi: 10.1016/j.jad.2022.03.028. Epub 2022 Mar 15. PMID: 35301041

Abstract:

Background: Yoga has several mechanisms that make it a promising treatment for depression and anxiety, including physical activity, behavioural activation, and mindfulness. Following positive outcomes from adapted CBT interventions incorporating mindfulness-based practices, this study explored the effects of a therapeutic yoga program as an adjunct to group-based CBT for depression or anxiety.

Methods: This was a pragmatic preference trial involving adults diagnosed with depression or anxiety in a regional primary mental healthcare service (n = 59), comparing transdiagnostic group CBT (n = 27) with transdiagnostic group CBT combined with an adjunct therapeutic yoga program (n = 32). A preference recruitment design allowed eligible participants (n = 35) to self-select into the adjunct program. The Depression Anxiety Stress Scale-21 (DASS) was assessed at baseline, post-intervention, and three-months follow up.

Results: CBT + Yoga was an acceptable alternative to CBT alone. Significant reductions were observed in total DASS scores and the 3 subscales of the DASS for both groups, however CBT + Yoga showed significantly lower depressive and anxiety symptoms post-intervention, compared to CBT alone. CBT + Yoga also showed sustained reductions in depressive symptoms over three-months, and more rapid reductions in depressive symptoms, compared to CBT alone.

Limitations: These findings should be considered preliminary due to the moderate sample size, with a rigorous randomised control trial necessary to definitively support the integration of yoga within mental health care to augment the benefits and uptake of transdiagnostic CBT for depression and anxiety.

Conclusions: Complementing other mindfulness-based practices, therapeutic yoga shows promise as an adjunct to transdiagnostic CBT.

Pal A, Nath B, Paul S, Meena S. Evaluation of the effectiveness of yoga in management of premenstrual syndrome: a systematic review and meta-analysis. J Psychosom Obstet Gynaecol. 2022 Jun 13:1-9. doi: 10.1080/0167482X.2022.2086457. Online ahead of print. PMID: 35697020

Abstract:

Aim: The management of Premenstrual Syndrome (PMS) is still evolving due to the modest effect sizes of the available treatment modalities. Yoga as therapeutic intervention in PMS has been gathering interest amongst researchers. The current manuscript reviews the evidence surrounding yoga in PMS.

Methods: This manuscript was a systematic review and meta-analysis evaluating the effectiveness of yoga on the total scores and sub-domains of PMS after studies were identified using a pre-defined selection criterion after a search in PubMed, Google Scholar, Scopus and Web of Science. Both quantitative and qualitative analysis of the accumulated data was performed. Overall, 14 studies were identified for the review, 11 of which were used for the purpose of quantitative analysis.

Results: The studies were heterogeneous in terms of the design, yoga regimes, nature of interventions and tools used for outcome measures. It was found that yoga was beneficial in the management of PMS. This benefit was also seen when all the sub-domains of PMS were individually examined except physical sub-domain.

Conclusion: Though there were certain limitations in our review like heterogeneity in studies, possibility of publication bias and restrictive selection criterion; it supported that yoga can be beneficial in patients with PMS.

Parajuli N, Pradhan B, Bapat S. Effect of yoga on cognitive functions and anxiety among female school children with low academic performance: A randomized control trial. Complement Ther Clin Pract. 2022 Jun 5;48:101614. doi: 10.1016/j.ctcp.2022.101614. Online ahead of print. PMID: 35688056

Abstract:

Background: To achieve better academic performance, students should improve their cognitive faculties and overcome anxiety. Therefore, the present research was conducted to assess the effect of yoga on the cognitive functions of female adolescents with low academic performance.

Methods: The present study is a randomized control trial (RCT). Eighty-nine female students in the age range of 12-14 years were randomly assigned into two groups [yoga (n = 45); physical exercise (n = 44)] at a school setting. Both groups were assessed before and after on Raven's standard progressive matrices (RSPM), Corsi Block Tapping Test (CBTT), Six Letter Cancellation Test (SLCT), Digit Letter Substitution Test (DLST), Stroop Color and Word Test (SCWT), and State-Trait Anxiety Inventory for Children (STAIC).

Results: Findings of the present study showed significant ($p < .05$) differences in scores of forward CBTT, SWCT, and SLCT in group \times time interaction. Both the groups showed significant ($p < .05$) improvement in SLCT, backward scores of CBTT, and STAIC-T. All outcomes measured were significantly ($p < .05$) improved in the yoga group except STAIC-S.

Conclusion: Yoga improves general intelligence, visuospatial working memory, and attention, as well as reduces the anxiety of students with low academic performance. Similarly, physical exercise was also found to be improving visuospatial working memory, sustained attention, and reduce trait anxiety. However, the finding of the present study indicated yoga to be more effective compared to physical exercise in regards to students' fluid intelligence and executive function. Improvement in general intelligence, visuospatial working memory, and attention is expected to positively influence students' academic performance.

Pirson L, Luer SC, Diezi M, Kroiss S, Brazzola P, Schilling FH et al. Pediatric oncologists' perspectives on the use of complementary medicine in pediatric cancer patients in Switzerland: A national survey-based cross-sectional study. Cancer Rep (Hoboken). 2022 Jun 14:e1649. doi: 10.1002/cnr2.1649. Online ahead of print. PMID: 35699504

Abstract:

Background: There is a widespread use of complementary therapies among pediatric cancer patients. Previous studies provided evidence that communication between pediatric oncologists (POs) and patients/families about the use of these therapies is often incomplete. Furthermore, nationwide studies on this topic are rare.

Aims: We assessed POs' perspectives on the use of complementary medicine (CM) in Switzerland, on the basis of an edited survey previously used in a nationwide study.

Methods and results: A link to an online survey was sent by e-mail to each of the fifty-two eligible pediatric oncologists in all nine Swiss Pediatric Oncology Group (SPOG) centers. Eligible respondents were board-certified (Switzerland or abroad) POs currently working at a SPOG center. The survey was available for a total period of 2 months. We received 29 filled questionnaires (overall response rate: 56%). Most POs (59%) indicated that they ask more than 50% of their patients about CM use. Frequent reasons for not asking about the use of CM were i) forgetting to ask (55%), ii) lack of knowledge on the subject (31%), and iii) lack of time (24%). More than every second PO (55%) reported having a lack of knowledge on the subject. A majority of POs (66% to 76%) indicated interest in learning more about specific CM topics (cannabinoids, hypnosis and relaxation, music therapy, herbal medicine, acupuncture, meditation, and yoga). More information and specific training opportunities on the use of CM was deemed important by 76% to 97% of POs.

Conclusion: POs working in Switzerland identify complementary therapies as an important subject. Swiss POs are willing to acquire more knowledge on CM. More training seems to be necessary in order to increase awareness about the

topic, to enhance communication about complementary therapies and thus to improve patient care.

Rajagopalan A, Krishna A, Mukkadan JK. Effect of Om chanting and Yoga Nidra on depression anxiety stress, sleep quality and autonomic functions of hypertensive subjects: A randomized controlled trial. J Basic Clin Physiol Pharmacol. 2022 Jun 13. doi: 10.1515/jbcpp-2022-0122. Online ahead of print. PMID: 35689170

Abstract:

Introduction: Hypertension (HTN) is a common and growing public health challenge with severe risk factors. Hence, this study aimed to assess the effect of Om chanting and Yoga Nidra on depression, anxiety, stress, sleep quality and autonomic functions on individuals with hypertension.

Methods: This prospective randomized controlled study was conducted in patients with hypertension at Little Flower Medical Research Center. A total of 80 patients with diagnosed hypertension were recruited and randomized equally to either the experimental group or control group. The experimental group received a combination of Om chanting and Yoga Nidra for five days a week for two months. The control group participants continued with their regular conventional medications. Depression anxiety stress scale (DASS), Pittsburgh sleep quality index (PSQI) and heart rate variability (HRV) scores were assessed at baseline, 30 and 60 day for both the groups.

Results: A total of 34 subjects in the experimental group and 31 subjects in the control group were included in the analysis. There was a significant ($p < 0.001$) reduction in depression, anxiety, stress, and a significant ($p < 0.001$) improvement in PSQI and HRV parameters in the experimental group was observed as compared to the control group. No adverse events were reported during the trial period.

Conclusions: The current study validates the effectiveness of Om chanting and Yoga Nidra in reducing depression, anxiety, stress and improving sleep quality and autonomic functions in hypertensive patients. These interventions could thus be considered a safer form of complementary therapy in managing stress and hypertension.

Sengupta J. Beyond Correct Postures and Flexible Bodies: Exploring the Relevance of Yoga in End-of-Life care. J Relig Health. 2022 Jun;61(3):2388-2397. doi: 10.1007/s10943-021-01317-3. Epub 2021 Jun 26. PMID: 34176066

Abstract:

Since the mid-twentieth century, Yoga has emerged as a multi-million US dollar global fitness industry. It has drawn worldwide followers to practice

postural and breathing techniques. However, the fitness model only elucidates how to live well and not how to die well. This article contends that the body-centric approach has little relevance to those who are dying. It espouses that yogic values like transcendence, holistic healing, harmony, and death-acceptance that qualify a 'good' death are regrettably lost in modern times. In conclusion, the soteriological aim needs to be retained in the modern yogic discourse to live well and die gracefully.

Souza LACE, Lima AA. Anthropometric, biochemical and clinical parameters in climacteric yoga practitioners. *Climacteric*. 2022 Jun;25(3):293-299. doi: 10.1080/13697137.2021.1965115. Epub 2021 Aug 23. PMID: 34423699

Abstract:

Objective: This study aimed to evaluate anthropometric, biochemical and clinical parameters in climacteric yoga practitioners.

Methods: This study investigated 108 climacteric women. We recruited 28 women between 40 and 65 years old who started yoga practices in premenopause and had already practiced for at least 5 years. As controls, we selected 30 physical activity (PA) practitioners who had practiced for at least 5 years and 50 sedentary women in the same age range. We conducted anthropometric, biochemical and blood pressure measurements.

Results: The yoga group had significantly lower fasting blood glucose than the PA practitioners and sedentary women. Yoga practitioners also had lower weight, body mass index, waist circumference, body fat percentage and waist-to-height ratio; higher levels of high-density lipoprotein cholesterol; lower levels of triglycerides, insulin, Homeostasis Model Assessment of Insulin Resistance, uric acid, apolipoprotein B and high-sensitivity C-reactive protein; and lower frequency of metabolic syndrome, lipid accumulation product, visceral adiposity index and systolic blood pressure than the sedentary women.

Conclusion: Yoga practitioners had lower glucose serum concentrations than the PA practitioners and sedentary women. Overall, the yoga group also had better anthropometric, biochemical and clinical variables than the other groups. Although further investigation is required, yoga practice in premenopause seems to be beneficial for women when they reach menopause.

Susanti HD, Sonko I, Chang PC, Chuang YH, Chung MH. Effects of yoga on menopausal symptoms and sleep quality across menopause statuses: A randomized controlled trial. *Nurs Health Sci*. 2022 Jun;24(2):368-379. doi: 10.1111/nhs.12931. Epub 2022 Mar 21. PMID: 35191141

Abstract:

This randomized controlled trial investigated the effects of yoga on menopausal symptoms and sleep quality across menopause statuses. Participants were randomly assigned to either the intervention or control group (n = 104 each), and those in the intervention group practiced yoga for 20 weeks. The participants completed the following questionnaires: the Depression, Anxiety, and Stress Scale; Multidimensional Scale of Perceived Social Support; Menopause Rating Scale; and Pittsburgh Sleep Quality Index. The results revealed that yoga effectively decreased menopausal symptoms, with the strongest effects noted in postmenopausal women (mean \pm standard deviation: 14.98 \pm 7.10), followed by perimenopausal women (6.11 \pm 2.07). Yoga significantly improved sleep quality in postmenopausal and perimenopausal women after controlling for social support, depression, anxiety, stress, and menopausal symptoms (p < 0.001). However, yoga did not affect sleep quality in premenopausal women. Overall sleep quality significantly improved in postmenopausal and perimenopausal women. Our data indicate that yoga can help decrease menopausal symptoms, particularly in perimenopausal and postmenopausal women, and improve their health.

Thulasi A, Kumar V, Jagannathan A, Angadi P, Umamaheswar K, Raghuram N. Development and Validation of Yoga Program for Patients with Type 2 Diabetes Mellitus (T2DM). J Relig Health. 2022 Jun;61(3):1951-1965. doi: 10.1007/s10943-019-00859-x. PMID: 31214846

Abstract:

This study with aim of development and validation of a yoga program for patients with T2DM was carried in view of emerging evidence of yoga as an alternative and/or complementary treatment. Classical and contemporary yoga texts were reviewed for identification of yoga practices. After reviewing research papers and yoga texts a THREE-step yoga program, in order of increasing difficulty level for T2DM was prepared. For validation of yoga program, mixed methods approach integrating qualitative and quantitative inputs was considered. Eighteen experts over three rounds of iteration contributed toward validation of yoga program. A final set of three-step yoga program was obtained which further needs to be tested in standardized randomized controlled trials. Trial Registration With Indian Council of Medical Research: Clinical Trial Registry of India; ICMR-CTRI: Development and Validation study: CTRI/2013/11/004163.

Truong MT, Nwosu OB, Gaytan Torres ME, Segura Vargas MP, Seifer AK, Nitschke M et al. Yoga Exercise App Designed for Patients With Axial Spondylarthritis: Development and User Experience Study. JMIR Form Res. 2022 Jun 3;6(6):e34566. doi: 10.2196/34566. PMID: 35657655

Abstract:

Background: Besides anti-inflammatory medication, physical exercise represents a cornerstone of modern treatment for patients with axial spondyloarthritis (AS). Digital health apps (DHAs) such as the yoga app YogiTherapy could remotely empower patients to autonomously and correctly perform exercises.

Objective: This study aimed to design and develop a smartphone-based app, YogiTherapy, for patients with AS. To gain additional insights into the usability of the graphical user interface (GUI) for further development of the app, this study focused exclusively on evaluating users' interaction with the GUI.

Methods: The development of the app and the user experience study took place between October 2020 and March 2021. The DHA was designed by engineering students, rheumatologists, and patients with AS. After the initial development process, a pilot version of the app was evaluated by 5 patients and 5 rheumatologists. The participants had to interact with the app's GUI and complete 5 navigation tasks within the app. Subsequently, the completion rate and experience questionnaire (attractiveness, perspicuity, efficiency, dependability, stimulation, and novelty) were completed by the patients.

Results: The results of the posttest questionnaires showed that most patients were already familiar with digital apps (4/5, 80%). The task completion rates of the usability test were 100% (5/5) for the tasks T1 and T2, which included selecting and starting a yoga lesson and navigating to an information page. Rheumatologists indicated that they were even more experienced with digital devices (2/5, 40% experts; 3/5, 60% intermediates). In this case, they scored task completion rates of 100% (5/5) for all 5 usability tasks T1 to T5. The mean results from the User Experience Questionnaire range from -3 (most negative) to +3 (most positive). According to rheumatologists' evaluations, attractiveness (mean 2.267, SD 0.401) and stimulation (mean 2.250, SD 0.354) achieved the best mean results compared with dependability (mean 2.000, SD 0.395). Patients rated attractiveness at a mean of 2.167 (SD 0.565) and stimulation at a mean of 1.950 (SD 0.873). The lowest mean score was reported for perspicuity (mean 1.250, SD 1.425).

Conclusions: The newly developed and tested DHA YogiTherapy demonstrated moderate usability among rheumatologists and patients with rheumatic diseases. The app can be used by patients with AS as a complementary treatment. The initial evaluation of the GUI identified significant usability problems that need to be addressed before the start of a clinical evaluation. Prospective trials are also needed in the second step to prove the clinical benefits of the app.

Vajpeyee M, Tiwari S, Jain K, Modi P, Bhandari P, Monga G et al. Yoga and music intervention to reduce depression, anxiety, and stress during COVID-19 outbreak on healthcare workers. Int J Soc Psychiatry. 2022

Jun;68(4):798-807. doi: 10.1177/00207640211006742. Epub 2021 Apr 5. PMID: 33818166

Abstract:

Aim: To investigate impact of Yoga and Music Intervention on anxiety, stress, and depression levels of health care workers during the COVID-19 outbreak.

Methods: This study was conducted to assess psychological responses of 240 healthcare workers during COVID-19 outbreak. We used Yoga and Music Intervention in normal and abnormal subjects based on Depression Anxiety and Stress Scale-42 (DASS-42).

Results: Of all 209 participants, 105 (50.23%) had symptoms of depression (35.88%), anxiety (40.19), and stress (34.92%) alone or in combination. The data suggest that there is significant improvement in test scores after intervention. Majority of persons with abnormal score exhibited improved DASS-42 score on combined interventions of Yoga and music compared to control group. Even subjects without abnormalities on DASS-42 score also showed improved DASS-42 scores in intervention (n = 52) group compared to nonintervention (n = 52) group.

Conclusions: Our findings highlighted the significance of easily available, simple, inexpensive, safe nonpharmacological interventions like Yoga and Music therapy to overcome stress, anxiety, and depression in present times.

Welford P, Osth J, Hoy S, Diwan V, Hallgren M. Effects of yoga and aerobic exercise on wellbeing in physically inactive older adults: Randomized controlled trial (FitForAge). Complement Ther Med. 2022 Jun;66:102815. doi: 10.1016/j.ctim.2022.102815. Epub 2022 Feb 7. PMID: 35143970

Abstract:

Objective: To compare the effects of yoga and aerobic exercise (AE) on wellbeing in physically inactive, but otherwise healthy older adults. A secondary objective was to assess and compare the frequency of adverse events associated with yoga and AE.

Design: Twelve-week, three-group, parallel randomized controlled trial with blinded follow-up assessment.

Interventions: Participants were supported to complete ≥ 3 Hatha yoga classes/week or ≥ 3 AE sessions/week. A wait-list control (WLC) group continued usual daily activities.

Main outcome measure: Change in wellbeing, assessed using the Satisfaction with Life Scale (SWLS) and Life Satisfaction Index-Z (LSI), at baseline and at 12-week follow up.

Results: In total, 82 adults (mean age 72.5 years, range 65-85, 77% female) were recruited. Of these, 27 were randomized to yoga, 29 to aerobic exercise and 26 to wait-list control. Medium-magnitude treatment effects (Hedges' g) were seen for yoga versus WLC and AE versus WLC (SWLS, $g = 0.65$ and 0.56 ; LSI, $g = 0.54$ and 0.54 , respectively). In per-protocol analyses, larger effect sizes were found (SWLS, $g = 0.72$ and 0.66 ; LSI, $g = 0.76$ and 0.76 , respectively). Adverse events were less frequent in the yoga group (6/27; 22%) compared to AE (10/27; 37%).

Conclusions: Among physically inactive older adults, participation in yoga or AE was associated with beneficial effects on subjective wellbeing when compared to a non-active control group. Yoga was associated with fewer injuries and may be especially suitable for older adults (DRKS 00015093).