

The 3rd Annual CCNM Research Day: Student Research & Innovation in Naturopathic Medicine



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Note: Correction added after original version published on March 1, 2019. We regret any inconvenience caused.

Abstract

The following are abstracts from the research competition at the 3rd annual CCNM Research Day hosted by the Canadian College of Naturopathic Medicine in Toronto, ON, Canada. The conference celebrates high quality student-faculty research collaborations, showcased as poster presentations.

Keywords: naturopathy; research; naturopathic medicine; complementary medicine; integrative medicine; undergraduate research competition; innovation; mentors

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Conference Abstracts

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Poster Presentations

A natural prescription for mental health: A narrative review

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Introduction: One in six adults in North America will experience depression in their lifetime, and it is frequently a co-morbidity to other health concerns. Effective, affordable treatments are needed to combat the rising prevalence of mental health challenges in both adult and pediatric populations. Studies indicate a steady decline in individuals spending time outside. This literature review assesses the current evidence of the impact of nature on mental health and provides practical clinical guidance with the goal of recommending prescriptions for time outside.

Methods: This literature review used the Cochrane Library and PubMed databanks with the search terms: “Interacting with nature”, “Nature and mental health”, “Nature-based”, “Forest therapy”, “Shinrin yoku” and “Forest bathing”. We excluded studies that involved horticultural therapy, wilderness therapy and green exercise. We included systematic reviews, meta-analyses, qualitative studies, clinical trials and cross-over studies that address the impact of nature on mental health. This process yielded a total of 88 unique studies. We excluded five editorial articles.

Results: Sixty-five of the eight-three studies ultimately included in this literature review indicated positive benefit on cognition, stress-reduction, and mental health. Many of the other studies identified physiologic changes commonly associated with stress reduction. Fifteen of the sixty-five studies indicated that fewer than thirty minutes in nature can have acute positive psychological benefit. We were unable to find data on the impact of cumulative time outside.

Conclusion: The collected data suggest that as little as thirty minutes of forest exposure can produce acute psychophysiological benefits. The main limitations of the literature reviewed are inconsistent quality of the studies and inconsistent inclusion of length of exposure. Future areas of research could focus on other forms of natural exposure and associated psychological benefits as well as the relationship of duration and frequency of time in nature on mental health over time. Modern humankind tends to view nature as a physical resource, one meant to build homes and create products, but what if nature was critical for our mental health? Nature prescriptions could become standard in all parts of the world, offering a tremendous possibility for mental health treatment that is cost-effective, accessible and with limited side-effects.

Berberine versus metformin: A narrative review on the exploration of their similarities and differences, specifically in the utilization of ovarian cancer

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Introduction: Although metformin is known as a first-line treatment for diabetes, this drug has also been explored for its anticancer effects in ovarian cancer. Berberine is a natural health product that has similar properties to metformin in its physiological action. This review compares and contrasts the clinical roles, as well as mechanisms for these two agents as applied to ovarian cancer.

Methods: Initially, the Cochrane Library was utilized to ensure a review regarding the topic of metformin and berberine on ovarian cancer was not previously completed. PubMed, ScienceDirect, and Medline were used to conduct different searches relating to both interventions, metformin and berberine, on conditions including: diabetes, hyperlipidemia, PCOS, hyperlipidemia, and ovarian cancer. The search parameters included clinical trials that were published between January 2008 and January 2018.

Results: There was an abundance of clinical trials of metformin for the conditions noted. Far fewer trials were found for berberine. In relation to ovarian cancer, there were 162 in vitro studies and 5 clinical trials found on metformin. In comparison, there were 13 in vitro studies on berberine regarding its anti-neoplastic effects in ovarian cancer. No clinical trials were found in our search.

Conclusion: There are similarities with respect to the mechanisms between which berberine and metformin act, particularly of relevance through the mTOR pathway in ovarian cancer. Further investigation and research is necessary to draw more definite conclusions regarding these two interventions on their anti-neoplastic effects and in particular for berberine.

The efficacy of *Zingiber officinalis* in chemotherapy-induced nausea and vomiting: An updated narrative review

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Introduction: Although chemotherapy is one of the most common conventional cancer therapies utilized, it produces a variety of side effects, such as nausea and vomiting, which hinders the patients' well-being, functionality and alters their energy and mindfulness of healing. In fact, it has been proven that the quality of life of patients is reduced to 20% in those who experience chemotherapy-induced nausea and vomiting (CINV). One of the purposes of integrative oncology is to incorporate alternative methods to resolve such adverse effects. *Zingiber officinalis* has been studied for its anti-emetic, anti-inflammatory, carminative, and circulatory actions, however, its efficacy in prophylactically resolving chemotherapy-induced nausea and vomiting remains unclear. This updated narrative review further investigates the efficacy of *Zingiber officinalis* in reducing the intensity and incidence of CINV.

Methods: A search containing the terms 'chemotherapy-induced nausea and vomiting, *Zingiber officinalis* was conducted in PubMed, KNOW Oncology database, and the Cochrane database. Since the last systematic review regarding this research question was published in 2013, only randomized, placebo-controlled trials were included in this study that had not been included in previous meta-analyses. Studies must have use a minimum dose of 0.15 g of *Zingiber officinalis* and used a sample size of at least 40 cancer patients with no other diagnoses that may affect nausea and vomiting. A total of six studies were included in this narrative review.

Results: Two studies found that breast cancer patients incorporating 250mg of *Zingiber officinalis* yielded significantly less severe vomiting and incidence, compared to placebo ($p < 0.05$). In another study, supplementation of *Zingiber officinalis* dosed at 500mg yielded a statistically significant decrease in vomiting and retching episodes as well as severity ($p < 0.05$). The largest clinical trial included in this review consisted of 576 cancer patients divided into 4 groups: placebo, 0.5g, 1.0g, or 1.5g of *Zingiber officinalis*. It was concluded that 0.5-1.0g of *Zingiber officinalis* yielded the most optimal outcomes of decreased reduction in CINV ($p = 0.0017, 0.036$, respectively). When integrating 1g of *Zingiber officinalis* to regular prescription of anti-emetic drugs, severity of CINV was reduced by 27.3%.

Conclusion: *Zingiber officinalis* is an herbal root, traditionally used as a remedy for gastrointestinal complaints, particularly nausea and vomiting. There are many proposed pathways that *Zingiber officinalis* is involved in, in regards to the mechanism in which it affects nausea and vomiting: anti-inflammatory, vestibular interaction, 5HT₃ modulation, and vasopressin regulation. In the previous systematic review done in 2013 on supplementation of *Zingiber officinalis* on CINV, authors concluded that there was no significant difference when compared to anti-emetics. However, this updated narrative review reveals that the best outcomes of reduced nausea and vomiting was found in patients who integrated *Zingiber officinalis* alongside a prescribed anti-emetic, rather than the use of these two interventions independently from each other, which was not previously studied in any systematic reviews thus far. It was also evident that 0.5-1g of *Zingiber officinalis* was the optimal dose which generated the most significant benefits to CINV. Integration of *Zingiber officinalis* to conventional anti-emetics is safe and should be considered to maximize positive outcomes, rather than a comparison of the efficacy of these two interventions independently. Based on available evidence, a dose of 0.5-1 g of *Zingiber officinalis* provides the best outcomes. Further research is needed to refine *Zingiber officinalis*' anti-emetic effect based on individual chemotherapeutic drugs and which pharmaceutical anti-emetics, when combined with *Zingiber officinalis* show improved outcomes.

The association between intestinal permeability, irritable bowel syndrome and autoimmune disease: A narrative review

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Introduction: Irritable Bowel Syndrome (IBS) is a chronic disorder characterized by abdominal pain, visceral sensitivity, and altered bowel movements. It has an incidence estimated to be 1.35-1.5%, and prevalence to be 11.2% worldwide. Many physiological changes are observed in IBS, including altered integrity of the mucosal barrier, low grade inflammation, and

microbial dysbiosis. A body of literature has demonstrated that these factors may result in increased intestinal permeability (IP) in a sub-population of IBS patients, resulting in abnormal passage of antigens from the intestinal epithelium. Recent research has uncovered an association between increased IP and the pathological development of Autoimmune Diseases (AD), which may pose as a new identified risk for IBS patients with IP. Although there is no known cause of AD, IP is currently a leading hypothesis. This review will therefore explore the association between increased IP specifically in the IBS phenotype and development of AD.

Methods: A literature search was performed using electronic databases, up until January 2019.

Results: Sixteen human studies from 1989 to 2018 demonstrated an association between various AD's and increased IP. Additionally, novel research in patients with IBS has identified auto-antibody expression against gonadotropin-releasing hormone (GnRH), suggesting that IBS may be of autoimmune origin itself. In line with this, one study also observed an increased incidence of IBS and GnRH antibodies in patients with Sjögren's Disorder.

Conclusion: These findings demonstrate that IP is a potentially influential factor that coincides with both IBS and AD independently. Preliminary research also indicates that IBS may have an autoimmune pathogenesis itself. Limitations to these studies include lack of consistency in IP screening, wide variety of AD presentation, and small sample sizes. Currently, there are no human studies that have examined the association of AD in an IBS population with IP, in which further research is required to investigate this association. In conclusion, these results demonstrate possible clinical significance towards screening for IP in patients with IBS, as a preventative measure for the long-term development of AD.

Is the fear of autism affecting the measles-mumps-rubella (MMR) vaccine uptake? A narrative review

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Introduction: A publication in 1998 by Andrew Wakefield, a British gastroenterologist, and his colleagues described twelve children who experienced the first symptoms of autism within a month after receiving the MMR vaccine. Although Wakefield's research was found to be fraudulent, the scare caused MMR vaccination rates to fall, putting children worldwide at risk of contracting measles, mumps and rubella. Despite multiple studies disproving links between the MMR vaccine and the development of autism, immunization rates in Canada are still suboptimal, with some provinces having trouble meeting the 95% target needed for herd immunity. In this narrative review, we summarize the results from the most recent studies on the link between the MMR vaccine and autism, as well as the degree to which fear of this link continues to impact vaccine hesitancy.

Methods: We performed two separate searches on MEDLINE; one with string terms "MMR vaccine and autism" with limitations placed on publication dates within the last 10 years, systemic reviews and meta-analyses which yielded four studies; and the other using the string terms "vaccine hesitancy and MMR and autism" with limitations placed on publications in the last 5 years yielded seven studies. The information acquired from these searches form the basis of this review.

Results: The systematic reviews and meta-analyses we analyzed and summarized looked at a variety of case-control, case-series and retrospective studies seeking the relationship between autism and the MMR vaccine. Ultimately, the authors of these reviews were able to conclude that there is no causal link between the administration of the MMR vaccine and the subsequent development of autism. Additionally, the data shows that a significant portion of vaccine-hesitant parents decide not to vaccinate their children with the MMR vaccine due to the misconception that the vaccine is linked to autism.

Conclusion: Despite evidence showing no causal link between the MMR vaccine and autism, public concern continues to persist. Vaccine hesitancy leads to decreased "herd immunity" and increases the risk of infectious diseases. The public should be made aware of the entirety of the information contained within this and other reviews, so that parents can make an informed choice when considering the MMR vaccine.

Colostrum supplementation to increase lean body mass with training: A narrative review

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Introduction: Bovine colostrum contains a variety of bioactive components including growth factors. Insulin-like Growth Factor 1 (IGF-1) is most abundant and is similar to human IGF-1 which is known to stimulate DNA and protein synthesis and cellular growth. Lean body mass includes weight of skin, organs, bones, total water, muscle mass and is associate with better health and performance, particularly when combined with training. Based on the results of clinical studies, bovine colostrum supplementation has potential to increase gains in lean body mass when combined with training.

Methods: A systematic search was conducted using the search terms Colostrum, Colostrum and Lean Body Mass as well as Colostrum and Lean Muscle Mass in the following databases: Cochrane, PubMed, MEDLINE, ClinicalKey and Google

Scholar. Articles were included if colostrum supplementation was the primary intervention, the population was healthy, exercise training was conducted and the control was whey protein. Articles were excluded if the patient population had known pathologies (i.e. short bowel syndrome); protein other than whey was used as a control (i.e. Soy) or no performance exercises were conducted during the trial supplementation. After applying the exclusion and inclusion criteria 7 articles were examined for this review.

Results: Oral bovine colostrum supplementation (20g TID) significantly increased cross sectional area ($P=0.05$) and circumference ($P=0.05$) (skin and subcutaneous fat) during training, however, increases remained similar to control by the end of the study period. Oral bovine colostrum supplementation (60g QD and 20g QD) with training did not significantly increase body mass or composition compared to controls with no significant differences in IGF-1 levels. Oral bovine colostrum supplementation (20g TID) with training increased weight ($P<0.01$) and lean body mass ($P<0.01$) significantly, similar to control ($P<0.01$). Oral Bovine colostrum supplementation (20g QD) with training increased bone-free lean body mass ($P<0.05$) compared to control. Oral bovine colostrum supplementation (20g TID) with training showed a significant increase in lean tissue mass, bone mineral content and decreased percent fat ($P<0.05$) similar to control with no significant differences in IGF-1 levels. Oral bovine colostrum supplementation mixed with control and with creatine had significantly ($P<0.05$) greater gains in body mass and DXA total scanned mass compared to control alone and subjects who consumed mixed colostrum and creatine had greater increases in fat free mass compared to colostrum mixed with control, all with training. Lastly, oral bovine colostrum supplementation (60g QD) with training increased both body mass and lean body mass significantly, similar to controls.

Discussion: Bovine colostrum has been traditionally used as an immune support with low quality evidence to support this therapy. A low number of studies with variations in quality exist for bovine colostrum and lean body mass. Conventional methods of increasing lean body mass involves exercise, increasing dietary protein, creatine, whey, whey isolate, casein, whole food extracted amino acids and possibly vitamin D and omega-3 supplementation. DEXA or MRI is most beneficial in collecting body composition data. Serum IGF-1 is an important marker to propose a possible mechanism for bovine colostrum. Bovine colostrum is higher in cost than traditionally used whey protein.

Conclusion: Due to the variations in controls and lack of overall standardization of the studies, it was difficult to definitively prove colostrum's effect on lean body mass, although minimal effects were documented. There were no elevations in IGF-1 when serum levels were tested and based off the research found, colostrum may increase lean body mass similar to whey protein, with no additional benefits. Further research is needed.

Oral supplementation of l-carnitine and its esters in male infertility: A narrative review

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Introduction: Infertility is defined as the inability to conceive after one year of unprotected sexual intercourse. Male-factor infertility is a causal in 20-30% of cases, and a contributing factor in 50% of cases. In this review, we evaluate the efficacy of L-carnitine and acetyl L-carnitine in male participants with sub-optimal semen parameters.

Methods: A thorough search of the literature yielded 16 studies, of which five were included.

The studies included 293 participants in total, with varying degrees of abnormal semen parameters. Semen parameters were evaluated after the treatment period in all studies.

Results: Of the 5 studies included, L-carnitine had a positive effect on sperm motility in 4 studies.

Conclusion: There are significant limitations in interpreting the results of these studies. The number of participants overall is small, and there is significant heterogeneity in the dosage of L-carnitine as well as the inclusion criteria for each study. L-carnitine and its esters play a role in improving sperm parameters and in particular improve total motility and progressive motility. There is a need for continued research to establish the optimal dosage and to determine safety in this population.

Understanding the contributions, roles and impact naturopathic doctors bring within integrative oncological healthcare teams: A study proposal

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Introduction: It is evident that integrative oncology practices and interprofessional healthcare teams are expanding. Naturopathic Doctors (NDs) play an important role in managing patients suffering from cancer. NDs are trained to provide cancer patients with safe and effective natural modalities and reduce cancer treatment related side effects. Nevertheless, the role of NDs in an interprofessional setting may be unclear for conventional practitioners or patients. The aim of this study proposal

is to better understand NDs contributions, roles and impact in these integrative cancer settings, both on a patient and practitioner perspective.

Methods: We will conduct a focus group discussion with oncology patients to gain their perspective on the integration of an ND in their care. In addition, we will formulate semi-structured interviews with NDs and the rest of the integrative healthcare team. We plan to interview as many patients, NDs and other healthcare providers at each integrative oncology clinic in Toronto, Ontario.

Results: We will analyse the data from the questions and the perspectives from all those interviewed using NVivo software and thematic analysis as the synthesis to illustrate the results. We will try to arrange the themes to focus on the following questions: How do NDs work together with the interprofessional healthcare team to achieve those outcomes efficiently and effectively? What is an ND's unique professional and personal contribution to the team? How can NDs facilitate the optimum functioning of the team and the best patient outcomes? What are the barriers you see that interfere with the proper integration of the NDs work with other health care professionals? What do you suggest to improve the integrative service that NDs can offer you to best manage your health issues? This project enables us to better understand the role of NDs in integrative oncology settings. The results will facilitate the expansion of this effective model of care in other integrative and interdisciplinary healthcare teams. This study will bring awareness to what NDs have to offer in interdisciplinary oncology healthcare teams and start the conversation of including them in these conventional settings.

Low glycemic index diet for pediatric refractory epilepsy: A narrative review

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Introduction: One third of all epilepsy cases fail to be controlled with seizure medication, leaving many parents looking to alternate therapies for their children. Refractory epilepsy may have significant long-term consequences for both the child and their caretakers. First line treatment for seizures, independent of age, is the use of anti-epileptic drugs (AEDs). Many patients with refractory epilepsy have been on at least two AEDs without becoming seizure free before they are termed to have refractory epilepsy. According to the Centers of Disease Control and Prevention, there are 150,000 new epilepsy diagnoses each year, with approximately 50,000 of these cases diagnosed in children and adolescents under the age of 18, resulting in an annual cost of approximately \$12.5 billion in the US each year, with 14% of this amount attributed to direct costs to the patient and 86% to indirect costs. The estimated prevalence of epilepsy is 2.2 million people or 7.1 for every 1,000 people. Currently, there are few studies that look to effective diet therapies with superior compliance, such as the low-glycemic index treatment (LGIT), as an effective alternative to the ketogenic diet (KD) to improve outcomes in pediatric epileptic patients.

Methods: PubMed and the Cochrane Database were searched using the terms "pediatric drug resistant epilepsy" AND "low glycemic index diet" published in English. Only RCTs, cohort, case-controlled, and meta-analyses were included in this analysis. Studies needed to use the LGIT in a pediatric population with refractory epilepsy. LGIT was outlined as 10% carbohydrate (40-60g carbohydrate/day), 30% protein, and 60% fat with glycemic index < 50. Studies were excluded if they did not meet the LGIT parameters, patient population, or condition. The search terms resulted in 210 studies of which 6 studies fit inclusion criteria. There were 2 clinical trials, 1 open-label prospective study, and 3 retrospective chart reviews included in this review.

Results: The majority of patients across all studies had a clinically and statistically significant (75-90%) reduction in seizure activity in less than 6 months and in a smaller percentage of participants, complete seizure freedom was achieved. All studies compared LGIT plus AEDs to AEDs alone. The studies showed that the LGIT is a safe and effective option for patients to reduce seizure frequency and is effective as a first dietary option for refractory epilepsy.

Conclusion: Study results were remarkable because in all reviewed studies, the LGIT shows to be an effective, more tolerable diet alternative to the strict KD and severe ketosis is not required. Some patients also experienced complete seizure freedom within 3 months, which is unable to be achieved with AED alone in refractory epilepsy. Research shows that ketosis alone does not account for a reduction in seizures. The LGIT mechanism of action may be due to the relationship between stable blood glucose and insulin levels, leading to seizure stability. Although there were differing limitations in each study, 5/6 studies showed no adverse effects from the LGIT and only 2 patients reported transient diarrhea. All studies in the review showed a correlation between length of diet adherence and increased outcomes, which could lead to selection bias. All studies used the same specific dietary recommendations for the LGIT as outlined in the inclusion criteria. Since all studies examined the addition of the LGIT to pharmaceutical therapy it is not possible to determine the effects of the LGIT alone in this population. As the number of refractory epileptic patients grow each year health care providers should be aware that research shows and supports effective and safe dietary treatment options, such as the LGIT to significantly decrease seizure activity with better adherence than the KD. More research is needed in order to determine longer term effects of the LGIT in order to fully determine its role in the treatment of refractory epilepsy.

Milk thistle as an adjunct therapy for chemotherapy induced hepatotoxicity: A narrative review

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Introduction: Chemotherapy-induced hepatotoxicity can be a dose-limiting side effect of cancer therapy. Dose reductions or premature discontinuation of treatment due to hepatotoxicity may increase risk of relapse and mortality; therefore, therapies to reduce this side effect have the potential to improve patient outcomes. Milk thistle (the active components of which are collectively called silymarin) is a herb traditionally used for liver conditions, and possess hepatoprotective and antioxidant properties. The objective of this poster is to review the available human literature for the use of milk thistle for prevention and treatment of chemotherapy-induced hepatotoxicity.

Methods: PubMed database and Cochrane Library were searched for human studies evaluating milk thistle supplementation for prevention or treatment of chemotherapy-induced hepatotoxicity. There were no language limitations; date range was from inception to September 30, 2018.

Results: Five papers were identified that met the inclusion criteria; three randomized controlled trials (RCT), one single arm pilot study, and one case report. The three RCTs found that treatment with milk thistle during or after chemotherapy administration significantly improved at least one marker of liver function as measured by liver function tests (LFTs) compared to placebo. The single arm pilot study found a statistically significant decrease in serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) and bilirubin when administered to individuals with grade 1 liver toxicity on regorafenib. The case study demonstrated an immediate decrease in LFTs after administration of milk thistle in a patient with chemotherapy-induced hepatotoxicity. Milk thistle was well tolerated. Although in vitro and pharmacokinetic data suggests that milk thistle is unlikely to interact with the efficacy of chemotherapy, human trials are needed properly evaluate.

Conclusion: Preliminary evidence suggests that oral administration of milk thistle preparations in patients receiving chemotherapy may reduce markers of hepatotoxicity. Milk thistle may protect the liver from oxidative stress and tissue damage caused by reactive oxygen species and cytokines due to its antioxidant, anti-inflammatory, and anti-carcinogenic actions. Larger RCTs are warranted to further evaluate the impact of milk thistle on chemotherapy-induced hepatotoxicity and treatment outcomes given the preliminary evidence reviewed.

Glycemic control using a ketogenic diet in type 2 diabetes: A narrative review

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Introduction: Type 2 diabetes mellitus (T2DM) is characterized as a metabolic disturbance that leads to elevated fasting and/or postprandial blood glucose due to insulin resistance. According to the American Diabetes Association, 30.3 million Americans were diagnosed with T2DM (9.4% of the population) in 2015 and nearly 1.5 million Americans are newly diagnosed each year. Additionally, the total cost of diagnosed diabetes is \$327 billion, making T2D a prevalent health and economic concern. Nutritional intervention is an integral part of treatment due to the strong parallel between obesity and T2DM. Current dietary standards recommended by the American Diabetes Association suggests a daily allowance of 130g of digestible carbohydrates per day; however, short-term studies and clinical trials have demonstrated improved insulin sensitivity and glucose management with reduction in total daily carbohydrate intake.

Methods: A search using the terms type 2 diabetes, HbA1c, and ketogenic diet was conducted in PubMed and the Cochrane database. Randomized controlled trials included in this review assessed HbA1c or fasting blood glucose levels and anthropometric measures in individuals with type 2 diabetes using the ketogenic diet as a treatment paradigm. Studies were excluded if participants were receiving insulin therapy or suffered from serious or unstable medical conditions. A total 27 studies were identified by the search terms; 6 randomized controlled trials were included in this review after applying the inclusion and exclusion criteria.

Results: Analysis of six randomized controlled trials demonstrated improvements in fasting blood glucose, HbA1c levels, and anthropometric measures with adherence to the ketogenic diet, which were significant compared to the minimal changes observed in T2DM patients in the control group. The trials consisted of small sample sizes ranging from 25 to 100 participants and durations varied from 4 to 12 months compared to baseline. Anthropometric measures including body weight, body mass index, and waist circumference, as well as fasting blood glucose and HbA1c levels, improved in all studies; however, reduction in HbA1c levels were independent of changes in body weight. A reduction in triglyceride levels and an increase in HDL cholesterol levels was also demonstrated in the ketogenic group. Two of the six randomized controlled trials evaluated adverse

events. Some common adverse effects of the ketogenic diet included asthenia, headache, and nausea and vomiting; however, no significant adverse effects were reported.

Conclusion: Type 2 diabetes mellitus is characterized as impaired glycemic control due to insulin resistance; thus, it results in reduced glucose uptake, which compromises the metabolism of dietary carbohydrates. The current nutritional standard for T2DM is a low-fat, moderate-carbohydrate diet, which has insufficiently improved clinical markers of diabetes, obesity, and cardiovascular risks. The ketogenic diet comprises of a high-fat, low-carbohydrate macronutrient content that induces transient ketone body levels in the blood and urine, also known as ketosis. A low-carbohydrate, ketogenic diet in individuals with T2DM can be beneficial for glycemic control, as well as other metabolic parameters, by providing an alternate fuel source due to impaired glucose metabolism. Improvements in these metabolic parameters – HbA1c, triglycerides, and body weight – can decrease the risk of comorbidities associated with the progression of T2DM such as cardiovascular disease, hypertension, and dyslipidemia. Limitations in the studies reviewed included small sample sizes, short durations, and high dropout rates in both intervention and control groups. Type 2 diabetes mellitus is the most common form of diabetes with an increase in prevalence world-wide. The strong relationship between dietary carbohydrates and postprandial serum glucose and insulin levels in individuals with T2DM warrants the investigation of carbohydrate restriction to improve serum values. Achieving dietary ketosis can result in clinically significant and beneficial metabolic outcomes in T2DM, including glycemic control and improved anthropometric measures. Future research is required to determine the long-term safety, efficacy, and adherence in larger sample sizes and studies of longer duration.

The effect of oral collagen supplementation on skin hydration: A narrative review

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Introduction: Dry skin, or xerosis, is a common condition that presents clinical and aesthetic challenges, in addition to being a significant predictor of dermatitis, eczema, psoriasis, pruritus, and sensitivity to external stimuli. Since xerosis is manifested on the skin, it is visible and can lead to aesthetic concerns from affected patients. Recently, oral collagen supplements have gained popularity as natural interventions for benefiting skin hydration. This review critically analyzes the literature surrounding the benefit of collagen supplements for skin hydration in the 30+ year old human population.

Methods: The search terms collagen supplement, skin hydration, and skin moisture were used in PubMed and Cochrane Library. Only randomized controlled trial studies (RCTs) with human subjects of 30 years and older were included. Porcine and fish-sourced oral collagen supplements were included. Trials assessing the efficacy of collagen alongside other nutraceuticals were excluded from the investigation. A total of 16 studies were identified by the search terms. After applying the inclusion and exclusion criteria, 9 studies remained and are included in this review.

Results: Skin Hydration All RCTs measuring hydration of the skin of the cheek or canthus demonstrated significant improvement from daily oral collagen supplementation. Two studies measuring the moisture content of the skin of the arm, did not observe significant improvement.

Collagen Dosage Dosage ranged from 1g to 10g of daily supplementation. As little as 1g had a significant increase in skin moisture. In comparing 2.5g, 5g, or 10g daily dosages, there was a dose-dependent increase in hydration; however, without statistical significance.

Source of Collagen Fish and porcine sources demonstrated significant improvement in skin hydration. One study found that while both sources significantly increase skin hydration, porcine-sourced collagen resulted in an earlier significant benefit compared to fish sources.

Duration of Treatment The earliest beneficial significant effect of collagen supplementation on skin hydration was after 4 weeks of daily supplementation.

Conclusion: The analyzed trials demonstrated a significant improvement in human skin hydration following oral collagen supplementation, but there was a small discrepancy in the results relative to specific location of the skin being measured (arm vs. face). In addition, the studies had small sample sizes; the smallest being 17 subjects, and the largest, 214. Further, the majority of the studies had conflicts of interest in the trials, as they were funded by nutraceutical companies with collagen products on the market. It is also important to note that the administration methods and instructions of collagen varied between the different collagen supplements being assessed.

Further research will be required to assess the discrepancy of collagen's effect on different skin locations, to further strengthen the causative relationship between collagen supplementation and skin hydration, and to further assess its efficacy for other clinical manifestations of xerosis, as in atopic dermatitis or psoriasis. Daily collagen supplementation is a natural intervention without any reported adverse effects that can improve skin hydration, and potentially improve and prevent xerosis. There is significant improvement found in overall skin hydration levels, but this data is more consistent for facial skin hydration. Further research is needed.

Does phosphatidylcholine supplementation increase strength in resistance-trained males? A review

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Athletes looking to enhance strength and muscle hypertrophy often turn to dietary supplements as an adjunct to their training and nutrition regime. However, few supplements have proven to be both safe and efficacious. Phosphatidylcholine (PC) is a phospholipid derived from soy and egg sources which has been shown to activate mammalian target of rapamycin complex 1 (mTORC1), a key regulator of skeletal muscle hypertrophy. As an mTOR activator, PC has the potential to act as an ergogenic aid for increased muscle size and strength. In this review of nine recent clinical trials (2012-2017) and one animal trial, strength-trained males supplemented PC for up to eight weeks in conjunction to resistance training programs. The strongest potential effects seemed to be for lower body strength with four trials showing statistically significant effects and two trials showing trends. For upper body strength, only one trial showed significant increases with another showing a trend. Three studies demonstrated significant improvements in lower body muscle hypertrophy and two additional studies showed trends. Dosage was variable throughout the studies, but the more robustly conducted studies with positive findings utilized a 750 mg per day dose. Even though no strong conclusions can currently be made regarding efficacy, the preliminary research on PC is generally positive. Additional larger, well-controlled studies are warranted to enhance practitioner confidence in prescribing this supplement. The authors declare that they have no conflicts of interest.

Evidence mapping of herbal and mushroom products warranting evaluation in integrative cancer care

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Introduction: We conducted an exploratory project to map out ‘signals’ of potential efficacy and safety of natural health products (NHPs) in integrative cancer care. Our intention was to narrow the scope of NHPs warranting further evaluation and subsequently perform targeted systematic reviews of the totality of evidence of these key NHPs used in integrative cancer care. These targeted systematic reviews will ultimately be used to guide the Patterson Institute’s future research agenda of developing best practice clinical guidance recommendations for the use of NHPs in clinical oncology care.

Methods: These signals were obtained solely from human controlled studies that had both positive and statistically significant results and were identified from systematic reviews published in MEDLINE from 2010-2017 in English. As this was an evidence mapping, we did not review non-significant or negative results, cover all adverse events, or appraise study quality. Our primary outcomes of interest emphasized hard endpoints of cancer treatment: mortality, treatment response, recurrence, metastasis, and stable disease. Secondary outcomes included any other outcome assessed: treatment side effects, cancer symptoms (pain, fatigue, appetite, quality of life), immune variables, and biomarker levels among others. Results were categorized by type of NHP, and key findings for single botanical and fungi preparations are presented herein.

Methods: In total across all NHP categories over 1950 records were screened and 218 reviews were included. Of the 218 reviews included, 69 reviews reported relevant results on single botanical and fungi preparations. Among these, 30 randomized controlled trials had positive significant results for our primary endpoints with sample sizes from 26 to 692. *Coriolus versicolor* (turkey tail) mushroom (including PSK/PSP polysaccharides), Mistletoe extract, *Panax ginseng* (including ginsenoside Rg3), and *Astragalus* were leading herbal and mushroom products for our primary outcomes. For secondary outcomes, key positive signals identified Cannabinoids, Ginger, *Brucea javanica* oil emulsion, and *Ganoderma lucidum* (reishi) mushroom.

Acknowledgements: This study was funded by the Patterson Institute for Integrative Cancer Research at CCNM. We gratefully acknowledge the tremendous support of our founding donors, John and Thea Patterson. We thank Dr. Nancy Rawling, BSc, ND for her valuable assistance.

Interim update from the first CCNM Innovation Fund Project: Scoping review of primary natural health products identified in the Integrative Pediatric Oncology Program (IPOP) Survey

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Introduction: A survey of the Oncology Association of Naturopathic Physicians (OncANP) membership was conducted over the past ~2 years asking about recommendations by naturopathic doctors (NDs) for pediatric cancer care. Eighteen primary health products (NHPs) were identified from this survey (selected by >50% of oncology focused NDs who treat children). A scoping review, supported by the CCNM Student Innovation Fund, was undertaken in order to map out the current body of evidence that exists for these identified recommendations.

Results: The methodology of the scoping review was formalised, based on the widely used protocol described by Arksey & O'Malley, with considerations incorporated based on Levac *et al.* Stage I (Identifying Research Questions) and Stage II (Identifying Relevant Studies) have been completed. A medical librarian conducted a peer-reviewed search strategy in databases including Ovid MEDLINE® ALL, Embase Classic + Embase, PsycINFO, and five databases from EBM Reviews (Central Register of Controlled Trials, Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Health Technology Assessment Database and NHS Economic Evaluation Database), from inception to October 2018. A total of 4750 deduped citations were found and initial inclusion/exclusion criteria have been formalised. Abstrackr® was selected as the platform for the initial screening at the title/abstract level.

Conclusion: We are currently working on Stage III of the scoping review. This involves study selection, beginning with a dual-screening process of titles/abstracts of citations collected through the systematic search. Results from this scoping review will allow us to map out the current state of available evidence with regards to applicable NHPs and pediatric cancer care. This will influence selections and considerations for the hospital based integrative pediatric oncology program (IPOP).

Vitamin D supplementation and its effects on insulin resistance in PCOS: A review

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Introduction: Polycystic ovarian syndrome (PCOS) is a common multifactorial endocrine disorder with a prevalence of 5-10% in reproductive-aged women. PCOS is characterized by irregular menses, polycystic or enlarged ovaries, and hyperandrogenism. Some other symptoms associated with PCOS are acne, hirsutism, glucose intolerance and insulin resistance. It is estimated that 31% to 35% of PCOS women have impaired glucose tolerance; and approximately 7.5 to 10% are diagnosed with diabetic mellitus. It is hypothesized that vitamin D supplementation influences metabolic profile including insulin sensitivity particularly in PCOS patients.

Methods: This systematic review aims to compare and summarize findings regarding the efficacy of vitamin D intervention on insulin resistant women with PCOS. Electronic search using PubMed database was used, and out of 455 papers, 5 primary published studies were selected from 2009-2015. The initial search in PubMed yielded 14 randomized control trials 17 clinical trials on vitamin D intervention.

Results: Two studies were included. A randomized control in which 28 women diagnosed on PCOS using Rotterdam criteria were randomly selected to placebo-controlled and vitamin D groups, and 22 women, 11 from each group, completed the study. Majority of the participants were vitamin D-deficient at baseline. In this study, 6 participants, 3 from the placebo group and 3 from the vitamin D group had normal vitamin D levels (>30 ng/mL), 7 participants from the placebo group were severely deficient (<20 ng/mL), while 8 participants from the vitamin D group were severely deficient (<20 ng/mL). In terms of Quantitative Insulin Sensitivity Check Index (QUICKI), there was no significant difference between the two groups, while there was a significant difference in the reduction in the 2-hour insulin level at 12 weeks in the vitamin D group. In addition, there was no significant difference in the 2-hour insulin or glucose from the placebo group. There was no significant difference between the placebo or the vitamin D group in measuring fasting insulin, fasting glucose, and other measures of insulin sensitivity including Homeostatic model assessment-insulin resistance (HOMA-IR). Another cohort study was retrieved in which PCOS women had higher fasting insulin levels, HOMA-IR, HOMA-β, testosterone and androstenedione levels and significantly lower 25(OH)D, QUICKI compared to control group. In this study, genotyping results revealed some correlations between certain gene allele and insulin sensitivity in PCOS women.

Conclusion: In summary, there was no significant difference in measures of insulin sensitivity between the placebo and vitamin D groups, however, a reduction in the 2-hour insulin was seen in the vitamin D group. So far, there has only been one double-blinded randomized study done on vitamin D status and metabolic disturbances in PCOS. Findings of similar studies suggest that vitamin D intervention can increase insulin sensitivity in women with PCOS; however, it is hard to draw a definite conclusion and more well-designed placebo-controlled randomized clinical trials are needed.

Examining the impact of Mediterranean-style diet on the progression of neurodegenerative disease: A detailed review

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Introduction: To understand the impact a Mediterranean diet has on reversing or slowing the progression of neurodegenerative disease based on its well-established cardioprotective effects.

Methods: A summary of intervention studies, observational studies, and meta-analyses on Mediterranean Diet (MeDi) or MeDi-style interventions for neurodegenerative disease (NDD) and NDD risk factors found using keywords “Mediterranean diet”, “neurodegenerative disease”, “Alzheimer’s disease”, “Parkinson’s disease”, “cognitive decline” in various databases. Participants: Healthy populations, populations at risk for NDD, or populations already diagnosed with NDD. Intervention: MeDi or modified MeDi-style interventions Outcome measures: Neurological concerns such as Alzheimer’s disease, Parkinson’s disease, mild cognitive impairment, cognitive decline, and mental status were measured, as well as specific anatomical changes.

Results: After investigation of the current research, a majority of the results concluded that an increased adherence to MeDi or MeDi-style interventions was able to significantly protect against and slow progression of NDD based on a reduction of known risk factors.

Conclusion: The previously well-established cardioprotective effects of MeDi are applicable in NDD due to the likely reduction of inflammatory markers associated with the diet. However, there is a lack of research regarding the existence and extent of these protective effects. There is a need for large-scale randomized controlled trials to further solidify this prospect before considering a MeDi-style diet as an approach for the regression of cognitive decline in NDD.

Dietary interventions for psychosis: A scoping review

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Introduction: Schizophrenia spectrum disorders (SSD) are a cluster of severe mental illnesses with a lifetime prevalence of 0.7%. Although the etiology of SSD is not fully understood, it is generally believed that genetic, biological and social factors contribute. It is known that nutritional factors influence the course of medical and metabolic illnesses in schizophrenia. However, uptake of such interventions is low. Currently, there are limited nutritional guidelines for mental health in general, and no guidelines exist for SSD specifically. This article seeks to identify and review the available evidence for dietary interventions for SSD. The main aim of this study is to assess dietary interventions for efficacy, safety, and feasibility as well as identify research gaps in this field and provide recommendations for future research.

Methods: This literature review is a sub analysis of a larger scoping review of nutrition and psychosis. The review used a priori search strategy encompassing three hundred search terms. Databases utilized included Embase, Embase Classic and Ovid MEDLINE. The present review included those studies that evaluated an intervention that modified the patient’s dietary pattern (rather than an individual food or constituent) and reported at least one mental health outcome.

Results: Twenty-seven articles were identified and reviewed. Of these, twenty-two implemented educational programs that supported healthy dietary changes, three studies implemented a stricter weight loss initiative or low calorie diet, and two studies used “various” techniques. Many of the studies supplemented the dietary intervention in combination with psychosocial initiatives or exercise. The specific details of the interventions were not generally well described but included food logs, and periodic individual or group support sessions. In most of the studies participants continued the use of their medications. Outcome measures included quality of life, mental health symptoms, weight/body mass index and biomarkers such as brain-derived neurotrophic factor. Seventeen articles showed positive direction of finding in terms of quality of life, symptom improvement, increased functioning, and/or improved cognition. However, none of the studies commented on how long these positive changes lasted for. The remaining studies showed no statistically significant changes in outcome variables. Adverse events were rarely reported but one study found that some participants increased their use of medication during the intervention and another study showed a decreased quality of life after the intervention.

Conclusion: Overall, these studies suggest that there may be value in dietary interventions for patients with SSD. Future research should delineate the exact details of the interventions more clearly and more studies should have mental health as the primary outcome. Additionally, studies should look at the effects of modifying diet alone to control for confounding variables such as medication and exercise. The feasibility of these types of changes in inpatient versus outpatient clinics should also be explored. There is some evidence to suggest that patients with SSD will benefit from dietary counseling and support providing rationale for further study.

Conflicts of Interest

The authors declare that they have no conflict of interests.

Authors' Contributions

MA and KC co-founded the first CCNM Research day.

JD, SH, QZ, MA, and KC contributed equally to planning of the research competition, assisted in the collection and review of the abstract submissions, as well as support for authors selected for the competition while producing their posters.

Acknowledgements

Special thanks to Julia Zander, Digital Media Specialist at the Canadian College of Naturopathic Medicine. Her patience, and keen, creative eye, were key to the creation of research posters for this competition. We would also like to acknowledge the work of our poster judging panel for their critical appraisal and scientific discussion on the day of the competition.

Funding

Funding for this conference has been supported by Biotics Research Inc. through an arms-length donation to the Canadian College of Naturopathic Medicine's Student Innovation Fund as well as an anonymous donor.

Article Information

Managing Editor: Jeremy Y. Ng

Article Dates: Received Feb 22 19; Published Mar 01 19

Citation

Please cite this article as follows:

Dertinger J, Hassan S, Zheng Q, Bhardwaj S, Aucoin M, Cooley K. The 3rd annual CCNM Research Day: Student research & innovation in naturopathic medicine. URNCST Journal. 2019 Mar 01: 3(3). <https://urncst.com/index.php/urncst/article/view/137>

DOI Link: <https://doi.org/10.26685/urncst.137>

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