

Brief Reports are generally shorter than full-length articles and are meant to communicate new data. For consideration in this section, pilot studies, brief evaluations, and reviews should present authoritative information on the integration of complementary and alternative therapies with conventional medical practices.

THE EFFECTS OF A SHORT PROGRAM OF DETOXIFICATION IN DISEASE-FREE INDIVIDUALS

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Context • Removal of toxins from the body is an integral part of Ayurvedic, yogic, and naturopathic medicine. Symptoms of poor health in people free from diagnosed disease may be related to toxin buildup.

Objective • This study investigates whether a 7-day program of detoxification can improve well-being and enhance the activity of liver detoxification pathways.

Methods • In this pilot, patient-outcome-focused, noncontrolled clinical intervention, 25 disease-free participants were recruited. Pre- and postmeasures were taken using the Metabolic Screening Questionnaire (as a subjective assessment of well-being) and drug challenge tests to assess hepatic detoxification capacity.

Results • A statistically significant (47%) reduction in the Metabolic Screening Questionnaire scores resulted. This improvement in patient-assessed health occurred concurrently with a 23% increase in liver detoxification capacity, as reflected by the caffeine clearance measure. There was an increase in the urinary sulfate-to-creatinine ratio after treatment, indicating a trend toward improved liver function.

Discussion • In disease-free adults, a 7-day course of detoxification may produce improvements in subjective health reports. This simple, short-term intervention may be appropriate for disease-free individuals without specific toxin exposure, for the purpose of enhancing health and preventing the development of disease.

Conclusions • A simple 7-day detoxification program resulted in a significant reduction in participant symptomology. The tendency toward improvement in liver detoxification measures is consistent with the hypothesis that improved liver detoxification capacity may contribute to well-being. (*Altern Ther Health Med.* 2000;6(4):70-76).

Detoxification typically means easing the “drying out” process of an alcohol or drug addict. Traditional systems of medicine with a philosophy based on understanding and applying the wisdom of nature have, as part of their therapeutic armamentaria, included techniques of detoxification.^{1,2} These medical systems include Ayurvedic, yogic, and naturopathic medicine. In this paper, detoxification indicates techniques that are designed to enhance removal of all toxins from the human body. Using the broadest definition, toxins include exogenously and endogenously produced substances that, if left in the body, may cause harm or promote illness.^{3,4} Toxins may be allergens, pesticides, herbicides, air pollutants, dioxins, recreational drugs, prescription drugs, and bowel toxins created from inappropriate gastrointestinal health.^{5,6}

Theoretically, the goals of a comprehensive program of detoxification include (1) decreasing exposure to known toxins, (2) increasing excretory functions to increase excretion of toxins that have been mobilized from adipose and extracellular matrix stores into blood, and (3) improving the liver’s ability to metabolize toxins. Examples of recommendations oriented to decreasing exposure to known toxins could include (1) changing residential or occupational conditions (ie, moving, if living next to a farm that is heavily sprayed with pesticides or in a new mobile home made of synthetic materials and glues), (2) eating organic foods as often as possible, and (3) enhancing intestinal barrier integrity to decrease systemic exposure to bowel produced toxins.⁷ To achieve enhancing excretory functions, possible recommendations include increasing filtered water intake to ensure adequate kidney filtration, increasing fiber intake to ensure at least 2 to 3 bowel movements daily, increasing exercise duration or intensity to increase sweating and to improve bowel function,^{8,9} and ingesting herbal cholegogues to enhance bile flow, because a variety of lipophilic toxins are excreted via bile. To achieve improvement of the liver’s ability to metabolize toxins, liver tonifying herbs could be tried or specific nutrient supplements could be prescribed to enhance hepatic metabolism of toxicants.

A number of different detoxification programs have been published in contemporary literature.⁹⁻¹³ One approach includes

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the use of a specifically designed medical food supplement to enhance the liver's ability to metabolize toxins.¹⁰ The medical food supplement (UltraClear) contains micronutrients and macronutrient proportions that are known to regulate hepatic detoxification pathways.^{11,14} The liver has 2 well-established pathways for the chemical alteration of toxic compounds. These 2 pathways are commonly referred to as phase I and phase II. Phase I involves the use of a group of microsomal P450 isoenzymes. These mixed-function oxidases usually involve oxidation, reduction, hydrolysis, hydration, and isomerization. The toxin is rendered more water soluble by these reactions and therefore more readily excretable (ie, less toxic). Phase I pathway enzymes are known to metabolize many drugs (eg, phenobarbital), petrochemical hydrocarbons, as well as steroid hormones such as estrogens and testosterone.^{15,16} Phase II pathways conjugate phase I metabolites or original toxins to more hydrophilic compounds. Substrates for phase II reactions include glutathione, glucuronide, glycine, sulfur, acetyl, and methyl groups. If these biotransformed products have a low molecular weight, they are eliminated via the urine. If the end products are of a high molecular weight, they are eliminated through the bile.

A variety of drugs have been used to determine the activity of these drug metabolism pathways. The test is conducted by administering a certain amount and type of drug and then collecting urine or saliva samples after a specified period of time. These samples are then tested for specific drug metabolites by high-performance liquid chromatography or some other quantitative analysis. The results are expressed as a percent of the total parent drug and metabolites, which are recovered. For example, acetaminophen is an excellent challenge to assess the activity of phase II reactions, whereas caffeine is used for measuring the activity of phase I reactions.^{17,18} In this study, caffeine and sodium benzoate were used to assess the activity of phase I and phase II reactions, respectively.^{19,20}

Contemporary studies of detoxification have focused on using a program of detoxification for a period of several weeks to months to treat poor health.^{9,11,12} This study was designed to test whether a short (7-day) detoxification program could reduce general symptoms of poor health in disease-free adults.

METHODS

An outcome-focused, noncontrolled, clinical intervention trial design was used. Twenty-five naturopathic medical students were recruited from a second-year nutrition class to undergo a 7-day detoxification program. The students ranged in age from 23 to 40 years old, and were all free of a specific, diagnosable disease.

The detoxification program consisted of consuming a hypoallergenic diet (Table 1), 6 scoops of a medical food supplement (UltraClear), and at least 2 quarts of filtered water daily. The nutrient composition of the food supplement is presented in Table 2. The participants were asked to make no other changes in their diets or exercise program.

Changes in well-being were assessed using a short symptom questionnaire, the Metabolic Screening Questionnaire (MSQ).

TABLE 1 Hypoallergenic diet guidelines

UltraClear program

For 7 days, take 2 scoops UltraClear (scoop inside container) mixed in 8 oz of liquid (eg, spring or filtered water, or 4 oz of water and 4 oz of unsweetened juice) 3 times daily.

Foods to eat day 1 to 3

No suspected allergens or intolerances, no dairy, no wheat, no concentrated sweets, no caffeine products, no alcohol, no eggs, and no oats.

Any fruits except citrus fruits can be added to UltraClear or UltraClear PLUS to make a smoothie.

Any vegetables (best steamed or raw) except tomatoes or potatoes.

Basmati white rice and legumes (Rice Dream). Do not eat beans that are difficult to digest; consider peas, lentils, and green beans.

Use nuts and seeds freely—except peanuts.

Flavorings may include organic butter, olive oil, high-quality sunflower or flaxseed oil for cold uses, and herbs and spices, except salt.

Optional foods day 4

Turkey and fish, other than shell fish, may be added, as well as grains such as buckwheat, millet, amaranth, quinoa, and brown rice.

This questionnaire was originally designed to be a succinct form of the Cornell Medical Index, concentrating on symptoms that might be related to toxicities.¹⁰ The MSQ is a useful measure of multisystem symptomatic level of poor health regardless of whether a specific diagnosis has been established. Bland et al¹¹ provide the most recent publication of the MSQ. The MSQ was administered 2 days before beginning the detoxification program and within 2 days of stopping the detoxification program.

Hepatic phase I and phase II pathway activity was measured by the caffeine and sodium benzoate challenge tests, respectively.^{19,20} Although these 2 challenge substances are used as markers for the activity of the 2 hepatic pathways, no single challenge substance can be used to assess the activity of each of the many different P450 isozymes or the many conjugation reactions that are considered phase II reactions. Participants did not consume caffeinated products the day before or the first day of the study. They then consumed 300 mg to 400 mg of caffeine, depending on body weight. Saliva was collected at 2 hours and 14 hours after the caffeine ingestion. Three grams of sodium benzoate were consumed at the same time as the caffeine. Urine was collected for 4 hours after the challenge and analyzed for hippuric acid (the main sodium benzoate metabolite) content. These tests were conducted 2 days before beginning the detoxification program and within 2 days of ending the detoxification program.

Intestinal permeability was measured as part of a more comprehensive assessment of detoxification capacity. If intestinal permeability is higher than normal, this provides a route for systemic entry of toxins originating in the gastrointestinal tract.^{21,22} Nutrients within the UltraClear powder may be helpful in promoting healing of damaged mucosal cells (eg, vitamin A).²³

TABLE 2 The nutrient composition of the dietary supplement

Contents	Amount
Calories	450
Protein	95 g
Carbohydrate	51 g
Fat	9 g
Fiber	6 g
Sodium	180 mg
Potassium	1260 mg
Vitamin B ₁	6 mg
Vitamin B ₂	6 mg
Vitamin B ₃	21 mg
Vitamin B ₆	10.2 mg
Vitamin B ₁₂	10.8 µg
Folic acid	240 µg
Pantothenic acid	10.5 mg
Biotin	405 µg
Vitamin C	900 µg
Vitamin A	15000 U
Vitamin E	324 IU
Calcium	600 mg
Magnesium	420 mg
Iron	10.8 mg
Zinc	30 mg
Copper	3 mg
Phosphorus	600 mg
Manganese	3.9 mg
Selenium	120 µg
Chromium	150 µg
Molybdenum	360 µg
Iodine	159 µg
L-glutathione	10 mg
L-cysteine	5 mg
N-acetylcysteine	5 mg

Intestinal permeability was measured by the double sugar challenge method. Small molecules such as the nonmetabolizable sugar mannitol are readily absorbed across the mucosal surface barrier. Larger nonmetabolizable sugars such as lactulose are normally excluded from systemic absorption by the integrity of the tight junctions between mucosal cells. The intestinal permeability test directly measures absorption of mannitol as a marker of malabsorption and lactulose as a marker of mucosal integrity or intestinal permeability. To perform the test, the study participant mixed premeasured amounts of lactulose and mannitol and drank the solution. The test measures the amount of lactulose and mannitol recovered in a 6-hour urine sample by high-performance liquid chromatography.^{24,25}

Pre- and posttreatment scores on each of the tested parameters were compared using Student *t* test; $P < .05$ was considered a significant difference. This study was done in accordance with the requirements and recommendations of the National College

of Naturopathic Medicine Institutional Review Board and was carried out with the ethical standards set forth in the Helsinki Declaration of 1975.

RESULTS

The MSQ scores reflect a significant ($P < .011$) reduction in total symptomatology over this 7-day period for the study participants. The average pretreatment score of 57.0 was reduced to a posttreatment average score of 30.3 (Figure 1), an overall reduction of 44%. These results indicate a statistically significant decline in overall symptomatology and improved sense of well-being.

The liver detoxification profile reflects the capacity of the liver to oxidize, reduce, or hydrolyze toxins (phase I) and to conjugate toxins or phase I metabolites (phase II), rendering them hydrophilic and thereby more excretable. Caffeine clearance increased by 53% over the 7-day treatment period (Figure 2), reflecting a positive trend in phase I detoxification capacity; however, this change was not statistically significant. The benzoate conversion increased by 9%, reflecting a nonstatistically significant improvement in phase II glycine conjugation capacity (Figure 3). The sulfate-creatinine ratio increased by 13% (Figure 4), indicating improved reserves of sulphur-conjugating nutrients and glutathione status.

Lactulose recovery was reduced by 37% following the 7-day detoxification program (Figure 5). This reduction did not reach statistical significance, but shows a tendency toward reduced intestinal permeability. Mannitol recovery was not different between pre- and posttreatment measures (Figure 6). The stable lactulose-mannitol ratio indicated no treatment effect of the

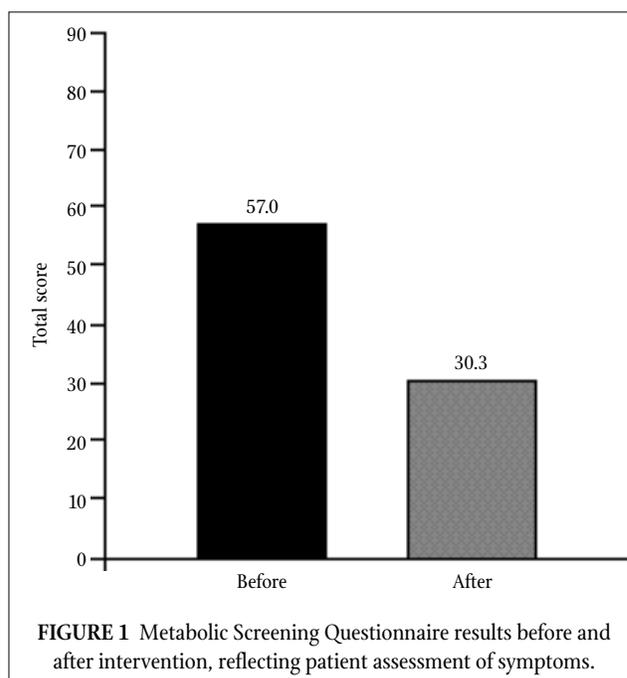


FIGURE 1 Metabolic Screening Questionnaire results before and after intervention, reflecting patient assessment of symptoms.

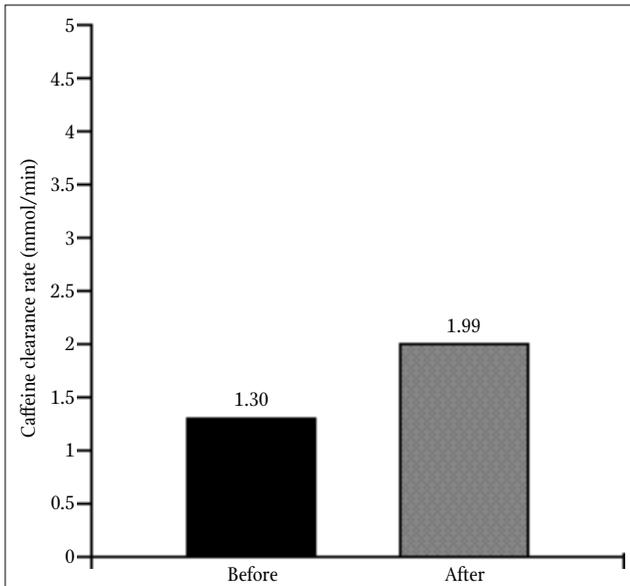


FIGURE 2 Hepatic cytochrome P450 A₁ activity before and after intervention. A marker for phase I detoxification activity.

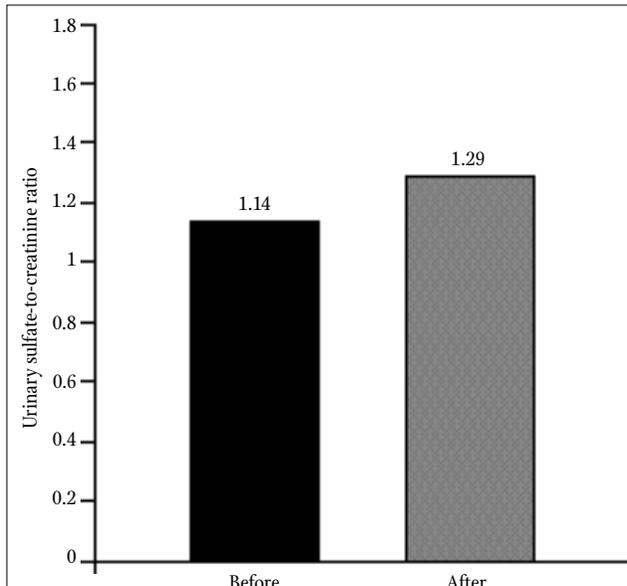


FIGURE 4 Urinary sulfate-to-creatinine ratio before and after intervention. A marker for sulfate levels. Sulfate is an important constituent of phase II detoxification pathways.

detoxification program on intestinal permeability. This result is not surprising because all study participants began the study with normal intestinal permeability.

DISCUSSION

A 7-day detoxification program combining a hypoallergenic diet and a medically designed food powder appears to decrease

symptoms of poor health. All laboratory measures showed improved detoxification capacity; however, the difference between pre- and postprogram measurements was not statistically significant. Due to the tremendous interindividual variability

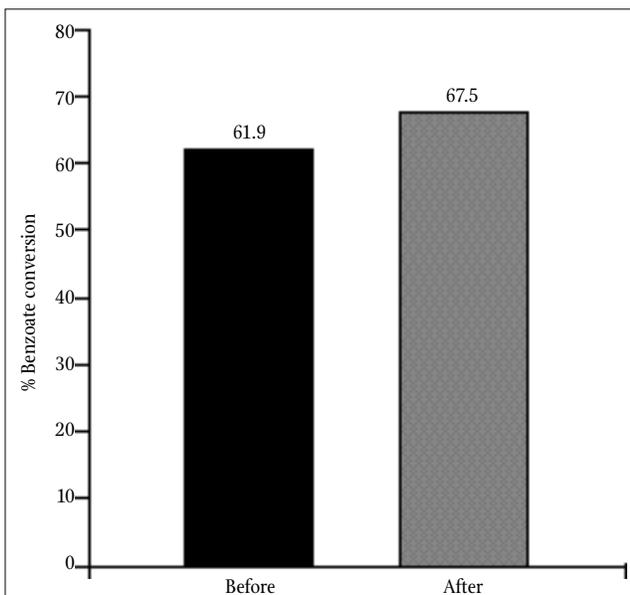


FIGURE 3 Hepatic glycine conjugation before and after intervention. A marker of phase II detoxification activity.

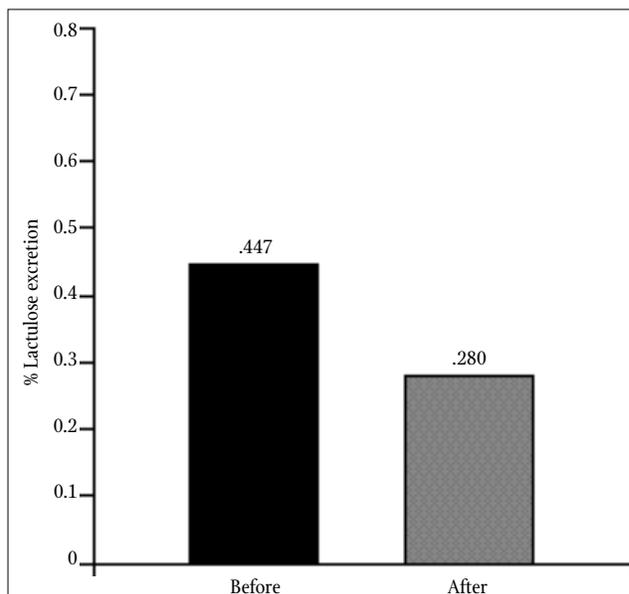


FIGURE 5 Lactulose challenge test results before and after intervention. Percentage of urinary lactulose recovery is a marker of degree of intestinal permeability. The greater the percentage recovery, the greater the intestinal permeability.

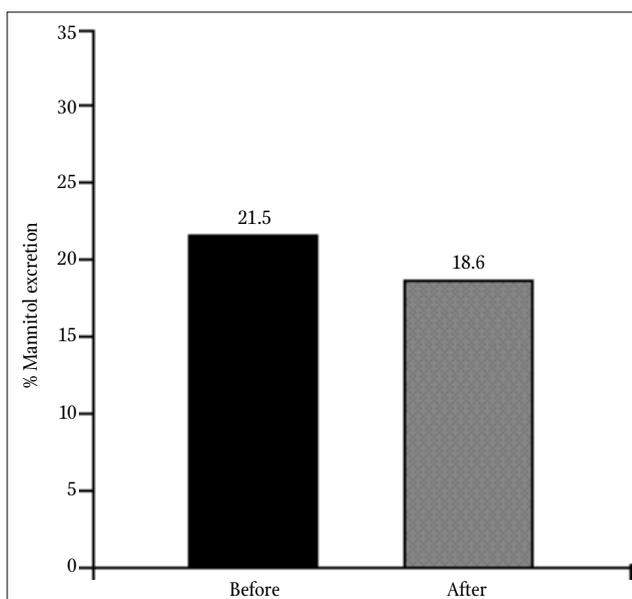


FIGURE 6 Mannitol challenge test results before and after intervention. Percentage of urinary mannitol recovery is used as a marker for malabsorption.

of measured activity of these hepatic pathways,¹⁷ the low symptomatology of the study participants (very symptomatic individuals generally score greater than 80-100 on the MSQ), and the short time of this detoxification program, the results in this study appear clinically significant. The favorable results of this small, pilot, outcome-focused study, the low possibility of adverse reactions with detoxification, and the large toxin burden inherent in an industrial society suggest that a periodic, weeklong program of detoxification might be an important public health measure.

The results of this study were similar to a 21-day study of this medically designed food supplement by Bland and Bralley.¹⁰ These researchers reported that a detoxification program led to significant improvements in MSQ scores (pretest mean of 47 versus posttest mean of 28), caffeine clearance, and benzoate clearance rates in 37 disease-free adults after 21 days of treatment.¹⁰ In this study, a significant reduction of overall symptomatology (pretest mean of 57 versus posttest mean of 30) was found with only 7 days of treatment. These findings suggest that when the detoxification program outcome is assessed by participant reports of well-being, only a weeklong program is necessary in nondiseased individuals. However, only after 21 days of treatment were significant differences found in biochemical assessments of detoxification capacity.¹⁰

Bland and Bralley¹⁰ suggest that changes in self-reports of well-being may be explained by a change in an individual's detoxification capacity. Because significant effects on symptom reduction but nonsignificant improvements in phase I and phase II activity were found in this study, the results do not confirm the

contention of Bland and Bralley. However, as Bland and Bralley¹⁰ point out, the individual variability of detoxification capacity is great, and this fact combined with the fewer subjects in this study could easily account for less than significant improvements in the metabolic assessment of treatment outcomes. The biochemical measures of detoxification tended in a direction supporting improved detoxification capacity, despite only 7 days of treatment.

A 2- to 3-week program of detoxification was reported to be effective for decreasing neurological symptoms associated with polychlorinated biphenyl exposure in 14 firemen.⁹ Neurophysiological and neuropsychological testing was conducted before and after the program of detoxification, which was initiated 6 months after polychlorinated biphenyl exposure. The detoxification program consisted of a "regulated diet," moderate aerobic exercise twice a day (30- to 60-minute bouts), and daily saunas. Since the "regulated diet" was not described in the study report, it is difficult to know what the authors were trying to accomplish. Clearly, the daily exercise and sauna were designed to enhance excretion of toxins. Some of the neuropsychological testing included questions found on the MSQ, reflecting assessment of subjective wellness. Despite the use of a significantly different detoxification approach, this report by Kilburn et al⁹ is in general agreement with the results of this study.

In another study, Bland et al¹¹ used UltraClear Sustain as the medical food supplement instead of UltraClear, and reported a 52% reduction in symptoms as measured by the MSQ. (Although similar, UltraClear Sustain was designed to improve gastrointestinal function, whereas UltraClear was designed to improve detoxification capacity.) Bland et al¹¹ conducted a study with 84 patients who had chronic health problems; the detoxification program lasted 10 weeks. The greatest improvement in these chronically ill patients (symptomatic with chronic fatigue syndrome, fibromyalgia, and irritable bowel syndrome for at least 1 year) occurred during the first 2 weeks of the detoxification program.¹¹ In the 7-day detoxification program reported in this article, the participants reported an average of 47% reduction in overall symptoms, whereas the patients in the UltraClear Sustain study had only a 27% reduction in symptoms for a similar time period. This difference is not surprising, because the individuals in this study (average initial MSQ of 56) would not be categorized as chronically ill patients (average initial MSQ of 77), and therefore it is reasonable to see a greater improvement in a shorter period of time.

In one study, a detoxification program consisting of daily aerobic exercise, daily saunas, daily massage, vitamin and mineral supplementation (some given intravenously and focusing on antioxidant nutrients), and large oral doses of niacin over 26 days led to symptom improvement in 86% of 210 chemically sensitive patients.¹² Similar to the study by Kilburn et al,⁹ this program of detoxification focused on enhancing excretion of toxins by promoting vasodilation (large doses of niacin) and sweating. Levels of volatile organic hydrocarbons were measured before and after the detoxification program; the blood levels decreased in 63% of patients.¹² The symptom improvement results of the

study in this article tend to confirm the results from the study by Rea et al,¹² despite a significantly different approach to detoxification. The questionnaire used in the Rea study for patient well-being was not published, but the researchers suggested that symptoms relating to mental and physical energy showed the greatest improvement.¹²

The few contemporary clinical studies that have used a detoxification approach to treat poor health have reported successful results. Each of these studies has employed one or more techniques in an effort to achieve one or more of the following theoretical goals of a detoxification program: (1) to decrease exposure to known toxins, (2) to increase excretory functions, and (3) to improve the liver's ability to metabolize toxins. Perhaps another important physiological goal for detoxification should be enhancing the mobilization of toxins from storage (eg, extracellular matrix and adipose tissue). This concept is considered important in Ayurvedic medicine's extensive use of detoxification therapies (Pancha karma).²⁶ Exercise, massage, and heating may help move toxins into circulation for chemical detoxification by the liver and subsequent excretion.

The most efficacious detoxification approach may depend on (1) the type of symptoms a patient is exhibiting, (2) an individual's capacity to metabolically detoxify xenobiotics, (3) the total toxin burden, and (4) the particular toxins to which an individual has been exposed. The most important elements for a periodic, prophylactic detoxification program for disease-free individuals may be the simplicity and ease by which the program may be accomplished. The approach used in this study compared to the detoxification programs used by Kilburn et al⁹ and Rea et al¹² has the advantage of less time and hassle and no need for special equipment (ie, a sauna). However, in those 2 studies, the subject population had known exposure to toxic hydrocarbon compounds that may be most rapidly and reliably eliminated by employing heating techniques.^{27,28}

The medical food supplement used in this study has been previously shown to regulate hepatic detoxification enzymes.¹⁰ One question that is raised when considering the results in this article is the importance of hepatic pathway upregulation compared to lessening an individual's toxic burden. These are both detoxification strategies; however, determining the simplest and least expensive approach to prophylactic, routine detoxification was the goal of this study. A follow-up study is planned to help clarify the need for a more comprehensive approach to detoxification compared to simply lowering the toxic burden using a hypoallergenic diet alone.

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