Maharishi Ayurveda

Summary of Research Findings

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Introduction

Maharishi Ayurveda is a comprehensive health care system with its roots dating back more than 5000 years to the ancient Vedic civilization of India. Ayurveda is translated as the 'Science of Life.' Maharishi Mahesh Yogi, founder of the Transcendental Meditation technique, recently established Ayurveda in its completeness in accordance with the classical texts, in association with Ayurvedic scholars, and made it available worldwide. Maharishi Ayurveda encompasses all facets of life, including mind (consciousness), physiology, behavior, and environment. It is prevention-oriented and also provides effective treatment modalities for chronic illnesses.

Maharishi Ayurveda uses various technologies for promotion of health and prevention of disease. These include diet, daily and seasonal routines, purification procedures, and use of herbal food supplements. During the last 30 years, there has been extensive research conducted on the various modalities of Maharishi Ayurveda. Over 600 studies have been carried out at more than 200 independent institutions and universities in 30 countries.
In addition, there are thousands of published studies on the wide-ranging health benefits of Ayurvedic herbs. Herein is presented a summary of research on Maharishi Ayurveda, focusing specifically on the studies conducted on Maharishi Ayurveda herbal formulas. This research demonstrates striking health benefits and profound possibilities for Maharishi Ayurveda in the health care field.

Maharishi Ayurveda herbal formulas nourish the natural structures and functions of the physiology rather than treating superficial symptoms, through the use of whole herbs that display the full range of biological intelligence. The ingredients of these herbal formulas function synergistically to maximize the health-promoting benefits. Maharishi Ayurveda herbal formulas combine time-tested wisdom from the ancient Ayurvedic texts with cutting-edge manufacturing and quality control technologies.

The ancient Ayurvedic texts teach *samyoga*—the science of combining various herbs into precise blends that offer the added value of synergy and balance. Maharishi Ayurveda formulas are not single herbs or random combinations of ingredients—they are carefully formulated combinations:

- Primary herbs strengthen specific functions of the mind and body.
- Bioavailability herbs improve assimilation.
- Herbal co-factors remove impurities that can block the full benefits of a formula.
- Balancing herbs cancel out any potential discomforts or side effects that may arise if you use individual herbs, rather than balanced combinations.

Equally important in Ayurveda is *sanskar*—preparing the herbs in such a way that the innate intelligence and healing wisdom of each plant is carefully preserved in the final product. Maharishi Ayurveda formulas are prepared meticulously according to the Ayurvedic texts. No short cuts are taken in preparation.

The Ayurvedic science of harvesting herbs standardizes the herb potency at its natural maximum without the use of chemical additives. Herbs naturally vary in potency with seasons, cycles of the moon, and time of day. Herbs used in the Maharishi Ayurveda formulations are harvested at their freshest in India. Where possible without threatening the natural ecological balance, Maharishi Ayurveda herbs are gathered in the wild, because wild-crafted herbs can be as much as 100 times more potent than their cultivated counterparts.

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The effectiveness of the Maharishi Ayurveda herbal preparations is assured by stringent quality control measures that include the following:

Expert herbalists. After the harvest, each type of plant must be inspected, sorted, cleaned, and stored in a particular way. Specialists in *Dravyaguna*—the identification of plant species—inspect each batch of plants. The whole batch is rejected unless it meets strict standards of purity and potency.

Herbal fingerprints. Each batch of plants is also inspected by a modern, government-recognized laboratory. The herbs are then tested using advanced technology such as high-pressure liquid chromatography (HPLC) to reveal the 'fingerprint' or exact species and potency of each herb.

State-of-the-art manufacturing. Advanced, hygienic processing facilities, designed by eminent vaidyas (traditional Ayurvedic physicians), scientists, and food technologists, incorporate the most modern technology in every aspect of the ancient Ayurvedic processes. This is the only ISO 9001 certified Ayurvedic production facility in the world. ISO certification is the international standard for assessing quality control in management, testing, and manufacturing.

Triple-tested for quality. High-tech scans are utilized for the detection of heavy metals, biological contaminants, and chemical residues. The ingredients are tested before preparation of the formulas, after manufacturing, and again by an independent lab, to exceed rigorous U.S. standards.

1. **Title**

Antineoplastic Properties of Maharishi-4 [MAK-4] Against DMBA-Induced Mammary Tumors in Rats

Publication

Pharmacology, Biochemistry and Behavior, Vol. 35, pp. 767-773, 1990.

Authors

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Summary

The herbal mixture MAK-4 (Maharishi Amrit Kalash-4) was tested for anticarcinogenic and anticancer properties against 7,12–dimethylbenz(a)anthracene (DMBA)-induced mammary tumors in rats. The 6% MAK-4-supplemented diet protected against DMBA-induced carcinogenesis by reducing both tumor incidence and multiplicity during initiation and promotion phases. MAK-4 provided up to 88% protection ($p<0.05$) during the promotion phase, and 60% ($p<0.05$) during the initiation phase of carcinogenesis. Also, 60% of the control animals which had developed fully-formed tumors showed tumor regression when their diet was subsequently supplemented with MAK-4 for four weeks. In 50% of these rats, the tumor regressed completely. There was no significant difference in the food intake or weight gain in rats on the MAK-4-supplemented diet compared to the control group

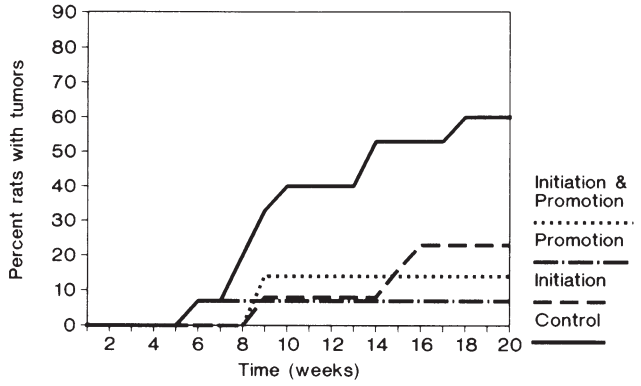

FIG. 1. Effect of 6% M-4-supplemented diet on tumor incidence. Tumor incidences in all groups were statistically analyzed using Chi-square test. C=60%, I=21%, P=7%, I&P=14%. I, P and I+P group were significantly different from C group ($p<0.05$).

TABLE 1.

CHANGES IN TUMOR VOLUME OF THE RATS IN THE REGRESSION GROUP TREATED WITH 6% M-4-SUPPLEMENTED DIET FOR FOUR WEEKS

Rat Number	Tumor Size (CM^3) 1st Week	2nd Week	3rd Week	4th Week	Change in Tumor Volume (CM^3)
1	0.36	0.21	0.03	0	−0.36
2	1.37	1.09	0.67	0.08	−1.29
3	3.16	4.63	6.78	6.78	+3.62
4	6.08	6.08	14.89	16.38	+10.30
5	0.30	0.11	0	0	−0.30
6	14.89	19.65	19.65	27.43	+12.54
7	5.32	6.78	9.84	10.97	+5.65
8	0.36	0.11	0.03	0	−0.36
9	0.36	0.01	0.01	0.01	−0.35
10	0.36	0.21	0.01	0.00	−0.36

+ Increase in tumor size.
− Decrease in tumor size.

Study 1 **Research Highlights**

A MAK-4-supplemented diet protected against DMBA-induced carcinogenesis in experimental rats by reducing both tumor incidence and multiplicity during the initiation and promotion phases. Subsequent MAK-4 supplementation produced partial to complete tumor regression in control animals.

2. Title

Antineoplastic Properties of Maharishi Amrit Kalash [MAK-5], An Ayurvedic Food Supplement, Against 7,12-Dimethylbenz(a)anthracene-Induced Mammary Tumors in Rats

Publication

Journal of Research and Education in Indian Medicine, Vol. 10, No. 3, pp. 1-8, July-September 1991.

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Summary

The herbal mixture Maharishi Amrit Kalash-5 (MAK-5) was tested for antineoplastic properties against 7,12-dimethylbenz(a)anthracene (DMBA)-induced mammary tumors in rats. The 0.2% (w/w) MAK-5-supplemented diet protected against DMBA-induced carcinogenesis during the promotion phase by reducing both tumor incidence and multiplicity. MAK-5 provided up to 62.5% protection ($p<0.05$) during the promotion phase of carcinogenesis. Also, a MAK-5-supplemented diet fed for four weeks to control rats which had developed mammary tumors, decreased tumor size in 60% of these rats. There was no significant difference in weight gain in rats on the MAK-5-supplemented diet. Thus, the MAK-5-supplemented diet did not influence the food intake, but protected against DMBA-induced mammary tumors in rats.

Study 2 **Research Highlights**

A MAK-5 supplemented diet protected against DMBA-induced mammary tumors in rats and supported tumor regression in control animals.

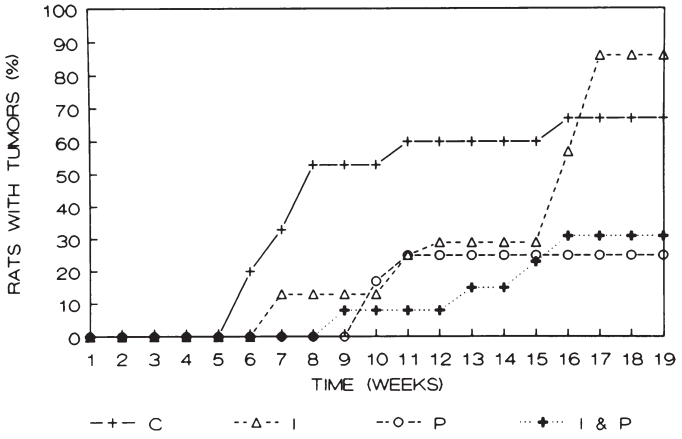

FIG. 2. Effect of 0.2% MAK-5-supplemented diet on tumor incidence. Tumor incidence in all groups was statistically analyzed using Chi-square test. The P and I+P groups were significantly different from C group ($p<0.05$). Groups: C=control; I=initiation; P=promotion; I+P=initiation and promotion.

TABLE 2.
CHANGE OF TUMOR VOLUME OF THE RATS IN THE REGRESSION GROUP TREATED WITH 0.2% MAK-5-SUPPLEMENTED DIET FOR FOUR WEEKS

RAT NUMBER	TUMOR VOLUME (CM^3) WEEK 1	WEEK 2	WEEK 3	WEEK 4	CHANGE IN TUMOR VOLUME (CM^3)
1	1.68	1.37	16.38	0.86	−0.82
2	3.70	4.00	10.97	19.65	+15.95
3	16.38	16.38	16.38	21.43	+5.05
4	0.36	0	0	0	−0.36
5	3.42	4.63	13.50	16.38	+12.96
6	0.86	0.36	0.36	0.36	−0.50
7	0.50	0.11	0	0	−0.50
8	1.37	0.88	0.86	0.66	−0.71
9	0.86	0.66	0.66	0.66	−0.20
10	0.86	2.05	2.05	2.92	+2.06

CM^3: CUBIC CENTIMETERS + : INCREASE IN TUMOR VOLUME
− : DECREASE IN TUMOR VOLUME

3. Title

Reduction of Metastases of Lewis Lung Carcinoma by an Ayurvedic Food Supplement [MAK-4] in Mice

Publication

Nutrition Research, Vol. 12, pp. 51-61, 1992.

Authors

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Summary

This study investigated the effect of oral feeding of an Ayurvedic rasayana (health-promoting/therapeutic herbal preparation) called Maharishi Amrit Kalash-4 (MAK-4) on metastasis of Lewis Lung Carcinoma (LLC) in mice. The mice were fed either chow containing 3% MAK-4 or standard laboratory chow, and inoculated subcutaneously with LLC tumor cells. After 4-5 weeks, the animals receiving the MAK-4-supplemented chow had a 65% reduction ($p<0.01$) in the number of metastatic nodules, and a 45% reduction ($p<0.01$) in the size of the nodules, compared to the control group.

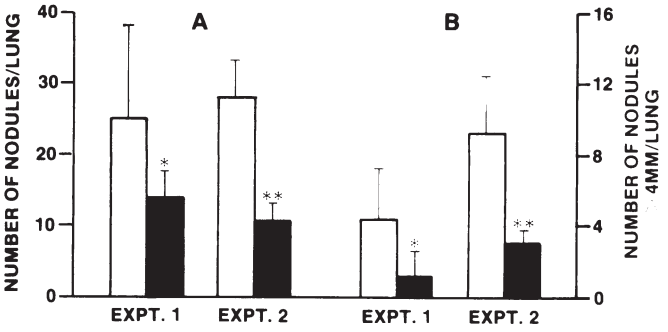

FIG. 1. Metastatic lung nodules (numbers/lung left side and size > 4 mm/lung right side) in animals on M-4-containing chow (Darkened Bars) and laboratory chow (Open Bars).
*P < .01 & **P < .001.

Study 3 **Research Highlights**
Mice fed MAK-4 supplemented diets experienced a significant reduction in both number and size of metastatic nodules.

4. Title

Ayurvedic (Science of Life) Agents [MAK-4 and MAK-5] Induce Differentiation in Murine Neuroblastoma Cells in Culture

Publication

Neuropharmacology, Vol. 31, No. 6, pp. 599-607, 1992.

Authors

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Summary

This study shows that an ethanol extract of MAK-5 (also known as Maharishi Amrit Kalash Ambrosia) induced morphological differentiation (neurite formation) and biochemical differentiation (increased activity of tyrosine hydroxylase by about 15-fold) in 75% of murine neuroblastoma cells in culture ($p<0.05$), indicative of reversal of the malignant process. An aqueous extract of MAK-5 increased only the activity of tyrosine hydroxylase and to a lesser extent than the ethanol extract. A treatment time of 3 days was needed for the expression of maximum differentiation. Ethanol and aqueous extracts of MAK-5 also increased the intracellular level of adenosine 3',5'-cyclic monophosphate (cAMP) by about 4-fold in 3 days. Ethanol extracts of MAK-5 also induced neurite formation in neuroblastoma cells grown in serum-free medium, but the concentration requirement was about a fifth of that needed in serum. A treatment time of 24 hours was sufficient to induce optimal differentiation in neuroblastoma cells grown in serum-free medium. The differentiating agents in the ethanol extract of MAK-5 were resistant to heat and light and could not be removed by treatment with activated charcoal. Neither the ethanol nor the aqueous extracts of MAK-4 (also known as Maharishi Amrit Kalash Nectar) induced differentiation in neuroblastoma cells.

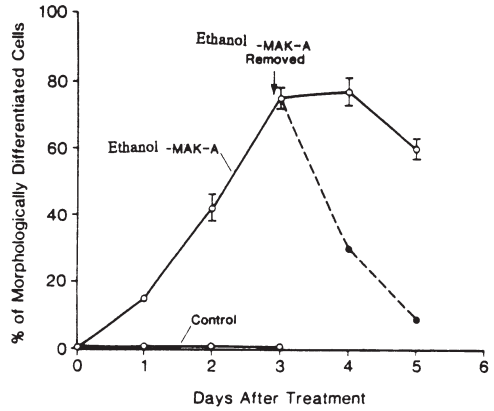

Fig. 2. Effect of an ethanol extract of MAK-A on morphological differentiation, as a function of treatment time. Ethanol-MAK-A (50 μg/ml) was added 1 day after plating. After 3 days of treatment, ethanol-MAK-A was removed and the number of morphologically differentiated cells was determined after 1 and 2 days of removal. Each value represents an average of 9 samples ± SEM. The sizes of bars for the SEM at some points did not exceed the size of the symbol; therefore, they were not represented.

Table 2. Effects of extracts of Maharishi Amrit Kalish-Ambrosia (MAK-A) on activity of tyrosine hydroxylase in neuroblastoma cells in culture

Treatments	Activity of tyrosine hydroxylase (pmol/hr/mg protein) 15 min	3 days
Control	8 ± 1*	8 ± 1
Solvent (0.2% ethanol)	—	17 ± 1**
Ethanol-MAK-A (50 μg/ml)	12 ± 1**	127 ± 9***
Ethanol-MAK-A (25 μg/ml)	—	25 ± 2***
Aqueous-MAK-A (170 μg/ml)	11 ± 1**	22 ± 4***
Aqueous-MAK-A (85 μg/ml)	—	16 ± 1**

Cells (0.25×10^6) for all groups, except those which received 50 μg/ml of ethanol-MAK-A and 170 μg/ml of aqueous-MAK-A; the latter were plated with 1×10^6 cells and were plated in tissue culture dishes (100 mm) and an ethanol extract and aqueous extract of MAK-A, were added separately 24 hr later. The medium and extracts were changed after 2 days of treatment and the activity of the enzyme was determined after 15 min and 3 days of treatment. Each value represents an average of 4 samples. Experiments were repeated 3 times and similar changes were observed in the treated groups, in comparison to controls.
*Standard error of the mean.
**Significantly different ($P < 0.05$) from control.
***Significantly different ($P < 0.05$) from solvent-treated control.

Table 3. Effects of extracts of Maharishi Amrit Kalish-Ambrosia (MAK-A) on the intracellular level of cAMP in neuroblastoma cells in culture

Treatments	Level of cAMP (pmol/hr/mg protein) 15 min	3 days
Control	13 ± 2*	11 ± 2*
Solvent (0.2% ethanol)	14 ± 1	15 ± 2**
Ethanol-MAK-A (25 μg/ml)	12 ± 1	23 ± 1***
Ethanol-MAK-A (50 μg/ml)	12 ± 1	47 ± 4***
Aqueous-MAK-A (85 μg/ml)	18 ± 2**	25 ± 2***
Aqueous-MAK-A (85 μg/ml)	19 ± 2**	42 ± 3***

Cells (50,000 cells for all groups except those which received 50 μg/ml and 170 μg/ml of ethanol-MAK-A, the latter were plated with 10^5 cells) plated in tissue culture dishes (60 mm) and an ethanol extract and an aqueous extract of MAK-A were added separately 24 hr later. The medium and extracts were changed after 2 days of treatment and the level of cAMP was determined after 15 min and 3 days of treatment. Each value represents an average of 3 samples. Experiments were repeated 3 times and similar changes were observed in the treated groups, in comparison to controls.
*Standard error of the mean.
**Significantly different ($P < 0.05$) from control.
***Significantly different ($P < 0.05$) from solvent-treated control.

Study 4 **Research Highlights**
An ethanol extract of MAK-5 induced morphological and biochemical changes in murine neuroblastoma cells in culture, indicative of a reversal of the malignant process.

5. Title

Anti-Tumor Effects of Natural Products Maharishi Amrit Kalash-4 (MAK-4) and Maharishi Amrit Kalash-5 (MAK-5) on Cell Transformation In Vitro and in Liver Carcinogenesis in Mice

Presented at

Nineteenth Annual Convention of Indian Association for Cancer Research and Symposium on Cancer Biology, Amala Cancer Hospital and Research Center, Thrissur, India, January 21-23, 2000.

Authors

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Summary

Background: Maharishi Amrit Kalash-4 (MAK-4) and Maharishi Amrit Kalash-5 (MAK-5) are herbal mixtures with anticancer and anticarcinogenic properties. This investigation evaluated the cancer-inhibiting effects of MAK-4 and MAK-5 in vitro and in vivo. Methods: Aqueous extracts of MAK-4 and MAK-5 were tested for effects on ras-induced cell transformation in the Rat 6 cell line assessed by focus formation assay. Urethane-treated mice were put on a standard pellet diet or a diet supplemented with MAK-4 and MAK-5. At 36 weeks, livers were examined for tumors, sera for oxygen radical absorbance capacity (ORAC), and liver homogenates for enzyme activities of glutathione peroxidase (GPX), glutathione-S-transferase (GST), and NAD(P)H: quinone reductase (QR). Liver fragments of MAK-fed mice were analyzed for connexin (cx) protein expression. Results: MAK-5 and a combination of MAK-5 plus MAK-4, inhibited ras-induced cell transformation. There was a 46% reduction in the number of mice that developed liver nodules when fed with MAK. MAK-treated mice had a significantly higher ORAC (two-sided $p<0.05$) compared to controls (200.2 ± 33.7 vs. 152.2 ± 15.7 ORAC units, respectively). MAK-treated mice had significantly higher activities of GPX, GST, and QR compared to controls (two-sided $p<0.05$, $p<0.01$, and $p<0.01$, respectively). Livers of MAK-treated mice showed a time-dependent increased expression of cx32. Conclusions: A MAK-supplemented diet inhibits liver carcinogenesis in urethane-treated mice. Possible mechanisms involving inhibition of oxidative damage and up-regulation of connexin expression are discussed.

Study 5 **Research Highlights**
A diet supplemented with MAK-4 and MAK-5 inhibited liver carcinogenesis in urethane-treated mice.

6. Title

Antineoplastic Properties of Dietary Maharishi-4 [MAK-4] and Maharishi Amrit Kalash [MAK-5], Ayurvedic Food Supplements

Publication

European Journal of Pharmacology, Vol. 183, No. 2, p. 193, 1990 (Abstract).

Authors
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Summary
Ayurveda (Ayu = life, Veda = knowledge, meaning the science of life) is an ancient medical science originated from Vedic tradition and widely practiced in India. Maharishi-4 (M-4) and Maharishi Amrit Kalash (MAK), ayurvedic food supplements belong to a group of substances known as rasayanas (Glazer, 1988).
In ayurveda, rasayanas are given to bring homeostasis in the physiology, retard aging, and enhance vitality and immunity (Sharma, 1985).

M-4 and MAK have been shown to inhibit 7,12-dimethylbenz(a)antracene (DMBA)-induced mammary tumors in rats when given individually as a dietary supplement (Sharma et al., 1989). The purpose of this investigation is to study the effectiveness of the combination of M-4 and MAK dietary supplementation on DMBA-induced mammary tumors in rats.

Fifty-day-old Sprague-Dawley rats were divided into 4 groups, having 20 rats in each group. Group 1 (C) and group 3 (P) were placed on a rodent chow diet (Wayne Research Animal Diets, Chicago, IL, USA). Groups 2 (I) and 4 (I and P) were placed on rodent chow supplemented with 6% M-4 and 0.2% MAK (provided by Maharishi Ayurveda Products International). All rats were given DMBA (75 mg/kg in 1 ml of sesame oil) by gavage after being on the diet for one week. One week after DMBA administration, the I group was placed back on the normal diet and the P group was placed on M-4 and MAK-supplemented diets. Rats were weighed and examined weekly for the presence of mammary tumors for a period of 20 weeks. In the other set of the experiment, animals with mammary tumors were placed on either M-4 or MAK-supplemented diets. Tumor size was measured once a week for 4 weeks. Histopathologies of tumors from different groups were also performed.

After 20 weeks of DMBA administration, the tumor incidence was 60, 30, 25, 15% in C, I, P, and I and P groups respectively; the average number of tumors per rat was 0.65, 0.5, 0.35, and 0.35 for C, I, P, and I and P groups respectively. M-4 and MAK-supplemented diets caused tumor regression in 60% of rats. There was no significant difference in weight gain of rats in all the groups. The tumors from the C group had adenocarcinomas. The tumors from the I and P groups showed adenocarcinoma with extensive fibrosis and focal areas of necrosis and calcification. The tumors from the I and P group showed lobular adenofibroma with inflammation.

These results indicate the M-4 and MAK-supplemented diets protect against DMBA-induced carcinogenesis. Similar results were observed when M-4 and MAK were supplemented in the diet individually at the same dosages. The combination of M-4 and MAK together in the diet does not produce synergistic effects.

Study 6 **Research Highlights**
MAK-4 and MAK-5 supplemented diets protected against DMBA-induced carcinogenesis in rats. Supplementing MAK-4 and MAK-5 individually at the same dosages achieved similar results as combined supplementation.

Research on Reduction of Chemotherapy Toxicity

1. **Title**

Antioxidant Adjuvant Therapy Using Natural Herbal Mixtures [MAK-4 and MAK-5] During Intensive Chemotherapy: Reduction in Toxicity. A Prospective Study of 62 Patients

Publication

Rao, R.S., Deo, M.G., and Sanghvi, L.D. (eds). Proceedings of the XVI International Cancer Congress. Bologna, Italy: Monduzzi Editore, 1994: pp. 3099-3102.

Authors

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Summary

The use of chemotherapeutic agents in the treatment of cancer is hampered and complicated by toxic side effects manifested by these agents. Many types of chemotherapy destroy cancer cells by generating free radicals, unstable molecules which can cause cellular damage. Unfortunately, these free radicals are not discriminatory in their destructive action, leading to undesirable side effects and sometimes even new cancers. In this clinical study, MAK-4 and MAK-5 were shown to be effective in reducing the toxic side effects associated with chemotherapy. This controlled prospective study was conducted on 62 patients undergoing intensive chemotherapy. The patients had various types of cancer, including non-Hodgkin's lymphoma, ovarian cancer, breast cancer, oral cancer, and osteogenic sarcoma. All patients were receiving combination chemotherapy; the chemotherapeutic agents included cyclophosphamide, vincristine, methotrexate, doxorubicin, prednisone, cisplatinum, adriamycin, and 5-fluorouracil. In the patients who received MAK-4 and MAK-5 along with their chemotherapy, there was reduced hemotologic toxicity, vomiting, and diarrhea, and improved sleep, weight, and an overall feeling of well-being. The patients taking MAK-4 and MAK-5 also showed a significant reduction ($p<0.03$) in lipid peroxide compared to the control group.

Study 1 **Research Highlights**

MAK-4 and MAK-5 supplementation was effective in reducing toxic chemotherapy side effects in patients undergoing intensive chemotherapy. Patients receiving the supplements experienced reduced hematologic toxicity, vomiting, and diarrhea, and improved sleep, weight, and well-being.

2. Title

Effects of Ayurvedic Food Supplement MAK-4 on Cisplatin-Induced Changes in Glutathione and Glutathione-S-transferase Activity

Publication

Rao, R.S., Deo, M.G., and Sanghvi, L.D. (eds). Proceedings of the XVI International Cancer Congress. Bologna, Italy: Monduzzi Editore, 1994: 589-592.

Authors

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Summary

Cisplatin, a chemotherapeutic drug used to treat testicular, ovarian, and other cancers, causes toxic side effects in the kidneys. A decrease in glutathione (GSH) and glutathione-S-transferase (GST) activities may play a role in this nephrotoxicity. This study on cisplatin and MAK-4 showed that cisplatin significantly decreases GSH and GST activity in both rat kidney and liver. Dietary MAK-4 supplementation reversed this effect of cisplatin on liver and kidney GSH and GST activity ($p<0.05$). Thus, MAK-4 may protect against cisplatin-induced toxicity in patients receiving this type of chemotherapy.

Table 1
Effects of cisplatin and M-4 treatment on GSH and GST levels in rat liver and kidney.

Group	Treatment	GSH (µg/g tissue) Liver	GSH (µg/g tissue) Kidney	GST (µmole/mg/min) Liver	GST (µmole/mg/min) Kidney
1	Control	11619±1574	4581±1125	1.91±0.5	1.47±0.2
2	Cisplatin	8899±1606*	2839± 920*	1.13±0.2*	1.18±0.3*
3	M-4	10942± 747	4495± 264	1.98±0.4	1.62±0.1
4	Cisplatin & M-4	10635±1262**	4374± 188**	1.86±0.4**	1.96±0.2**

*Significantly lower than control group (P<0.05)
**Significantly higher than cisplatin alone group (P<0.05)

Study 2 **Research Highlights**

This study on cisplatin and MAK-4 showed that cisplatin significantly decreased GSH and GST activity in both rat kidney and liver. Dietary MAK-4 supplementation reversed this effect of cisplatin on kidney and liver. Thus, dietary MAK-4 supplementation may protect against cisplatin-induced toxicity in patients receiving this type of chemotherapy.

3. Title

Protective Effects of MAK-4 and MAK-5 on Adriamycin-Induced Microsomal Lipid Peroxidation and Mortality

Publication

Biochemical Archives, Vol. 8, pp. 267-272, 1992.

Authors

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Summary

Use of the chemotherapeutic agent Adriamycin is complicated by its potentially lethal cardiac toxicity. DNA base pair damage induced by Adriamycin results in its effectiveness against cancer; however, simultaneous production of free radicals results in toxic side effects. In this study on mice, Adriamycin-induced mortality reached 60% in the control group (regular chow diet), compared to 20% in the group receiving a 6% MAK-4-supplemented diet ($p<0.05$), and 40% in the group receiving a 0.2% MAK-5-supplemented diet.

See Antioxidant Research for more information on this study.

Table 1
Adriamycin-induced Mortality*

Group	Mortality (%)
Control	60
M-4 (6%)	20
M-5 (0.2%)	40

*CDF_1 mice were treated with Adriamycin, 15 mg/kg, i.p. and animals were observed for four weeks for mortality.

Study 3 **Research Highlights**
Mice receiving the chemotherapeutic agent Adriamycin experienced a reduction in mortality when supplemented with MAK-4 or MAK-5.

4. Title
Maharishi Amrit Kalash [MAK-4 and MAK-5] Reduces Chemotherapy Toxicity in Breast Cancer Patients

Publication
Federation of American Societies for Experimental Biology Journal, Vol. 14, No. 4, p. A720, 2000 (Abstract).

Authors
A. Srivastava,* A. Samaiya,* V. Taranikanti,* P. Kachroo,* O.H. Coshic,* R. Parshad,* V. Seenu,* S. Chumber,* and M.C. Misra.*

Conducted at
* All India Institute of Medical Sciences, New Delhi, India 110029

and Title
Reducing the Toxic Effects of Chemotherapy: New Research Reports a Significant Decrease in Chemo Toxicity with a Natural, Ayurvedic Herbal Formula

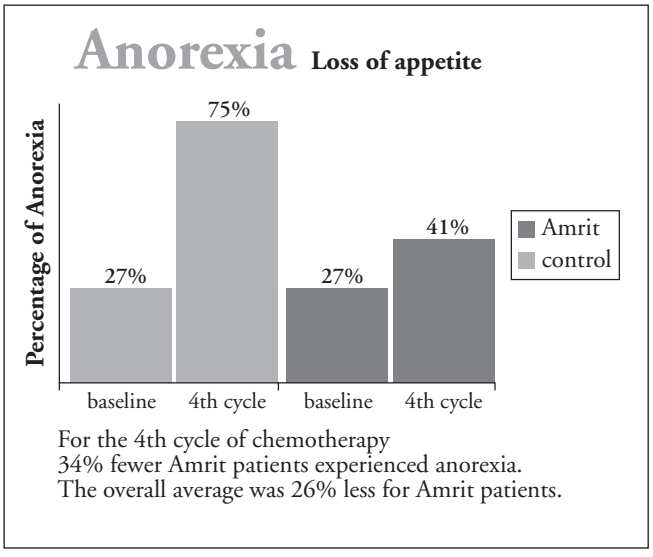
Publication
Townsend Letter for Doctors and Patients, August/September 2000, pp. 134-138.

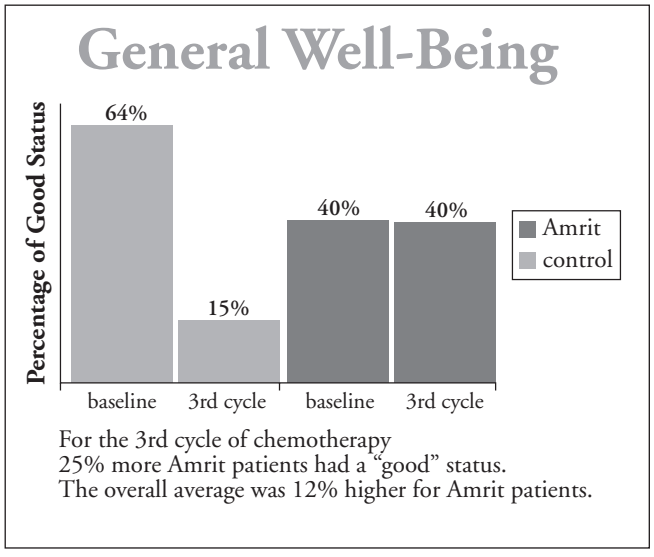
Author
John Thill.

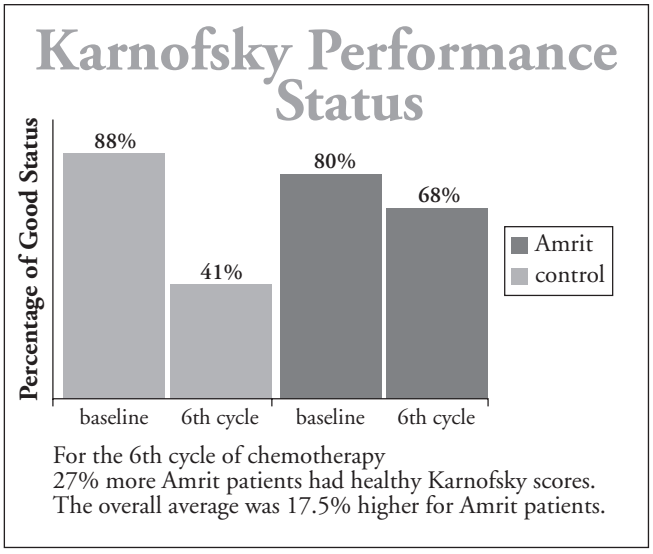
Summary

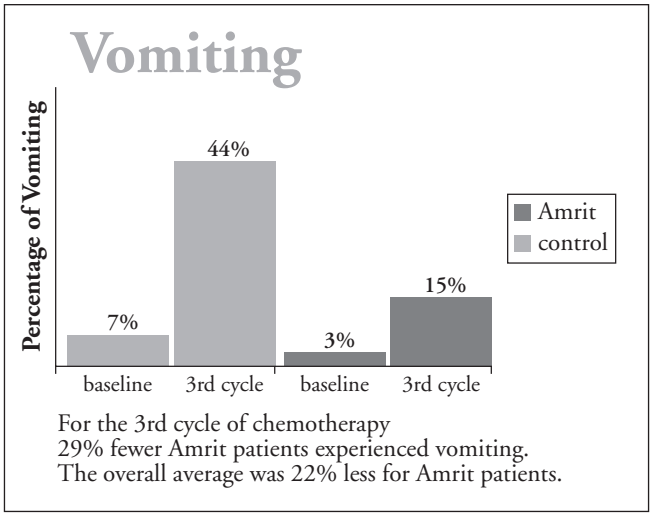
This randomized trial was conducted to determine the effect of the herbal mixtures MAK-4 and MAK-5 on reduction of toxic side effects in breast cancer patients receiving chemotherapy. There were 129 breast cancer patients (124 females and 5 males) involved in the study; 61 patients took MAK-4 and MAK-5 along with chemo-

therapy and 68 received chemotherapy alone and served as controls. There were two chemotherapy protocols used: cyclophosphamide plus adriamycin plus 5-fluorouracil (33 MAK patients and 32 control patients); and cyclophosphamide plus methotrexate plus 5-fluorouracil (28 MAK patients and 36 control patients). Patients received six cycles of chemotherapy at 28-day intervals and received ondansetron as an anti-emetic agent. Patients were evaluated for toxic side effects per World Health Organization (WHO) criteria. The mean age of the MAK patients and controls was similar: 43 ± 10 for the MAK group and 46 ± 9 for the controls. Results of the study showed improvement in several parameters for patients taking MAK as compared to controls: Karnofsky performance status, anorexia, vomiting, general well-being, and body weight. For the sixth cycle of chemotherapy, 27% more MAK patients had healthy Karnofsky scores, a scale that measures the ability to perform normal day-to-day activities. The overall average was 17.5% higher for MAK patients. For the fourth cycle of chemotherapy, 34% fewer MAK patients experienced loss of appetite (anorexia). The overall average was 26% less for patients taking MAK. For the third cycle of chemotherapy, 29% fewer MAK patients experienced vomiting. The overall average was 22% less for MAK patients. Also in the third cycle, 25% more MAK patients had a 'good' status of general well-being, with the overall average being 12% higher for MAK patients compared to controls. There was a statistically insignificant mean weight gain of 0.43 kg in the MAK patients, in comparison to a statistically significant mean weight loss of 1.12 kg in the control patients. Thus, patients on MAK were able to maintain their weight during treatment. Another important finding in this study was that there was no significant difference in tumor regression between the MAK patients and the controls. The MAK group had a statistically insignificant increase in the number of patients with tumor regression. This indicates that MAK does not impede the anti-cancer effects of chemotherapy. Thus, MAK is effective in reducing toxicity of chemotherapy treatment without impairing the anti-cancer effects of the chemotherapy.









Bar graphs reprinted with permission from Townsend Letter for Doctors and Patients, *August/September 2000, pp. 134-138, Tel. 360-385-6021.*

Study 4 **Research Highlights**
MAK-4 and MAK-5 supplemented diets were effective in reducing chemotherapy toxicity in breast cancer patients receiving chemotherapy and effectively supported weight maintenance. It also was found that MAK does not impede the anti-cancer effects of chemotherapy.

Research on Reduction of Chemical Toxicity

1. **Title**
Antioxidant Properties of Two Ayurvedic Herbal Preparations [MAK-4 and MAK-5]

Publication
Biochemical Archives, Vol. 10, pp. 25-31, 1994.

Authors
Stephen C. Bondy, Tina M. Hernandez, and Cara Mattia.

Conducted at
Department of Community and Environmental Medicine, University of California (Irvine), Irvine, CA 92717

Summary
Toluene is an organic solvent widely used in industry. Exposure to toluene can result in neuronal damage, as manifested by neurobehavioral and electrophysiological effects in humans and rats. Approximately six billion pounds of toluene are produced each year, therefore the potential for widespread occupational exposure is very high. In addition, toluene produces a euphoric effect which has led to its abuse. Toluene has been shown to induce excess oxidative activity within several organs, including the brain. In this investigation, ethanol and aqueous extracts of MAK-4 and MAK-5 were able to quench generation of reactive oxygen species (ROS) ($p<0.05$) within an isolated fraction of rat cerebral cortex enriched in mitochondria and nerve endings (synaptosomes). Based on these results, rats pretreated with MAK-5 showed a significant decrease in toluene-induced ROS in the cerebellar synaptosomal/mitochondrial preparations ($p<0.05$). Also, the alcoholic extract of MAK-5 significantly reduced toluene-induced ROS generation ($p<0.05$) in the kidney mitochondrial fraction.

See Antioxidant Research for more information on this study.

Fig. 3 Cerebellar ROS formation in toluene and MAK-5 treated rats

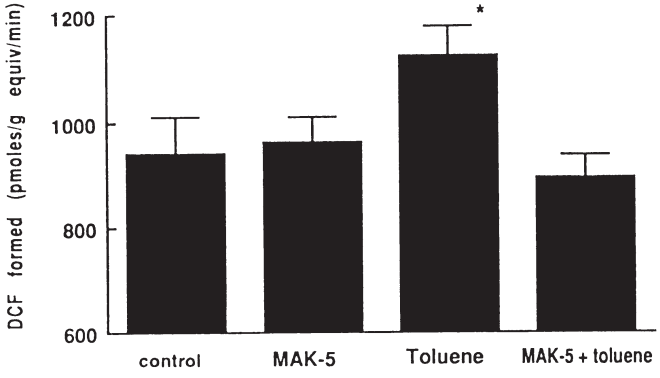


FIGURE 3
Cerebellar formation of reactive oxygen species in toluene- and MAK-5 treated rats Data are means ± SE derived from 6 animals/group. Experimental details in text. *: differs significantly from control value.

Study 1 **Research Highlights**
Rats pretreated with MAK-5 showed a significant decrease in toluene-induced reactive oxygen species (ROS) in cerebellar synaptosomal/mitochondrial preparations. Also, the alcoholic extract of MAK-5 significantly reduced toluene-induced ROS generation in the kidney mitochondrial fraction.

2. Title

In Vitro and In Vivo Inhibition of Microsomal Lipid Peroxidation by MA-631

Publication

Pharmacology, Biochemistry and Behavior, Vol. 48, No. 2, pp. 505-510, 1994.

Authors

Atef N. Hanna, Hari M. Sharma, Ellen M. Kauffman, and Howard A.I. Newman.

Conducted at

Department of Pathology, College of Medicine, The Ohio State University, Columbus, OH

Summary

MA-631 is an herbal mixture from the comprehensive system of natural health care known as Maharishi Ayur-Veda. The in vivo portion of this study on MA-631 involved feeding rats a 2% (w:w) MA-631-supplemented diet for three weeks, then challenging their system with an intraperitoneal injection of toluene. The results showed that the 2% MA-631-supplemented diet completely inhibited the in vivo microsomal lipid peroxidation induced by toluene in rat brain, kidney, liver, and heart ($p<0.05$).

See Antioxidant Research for more information on this study.

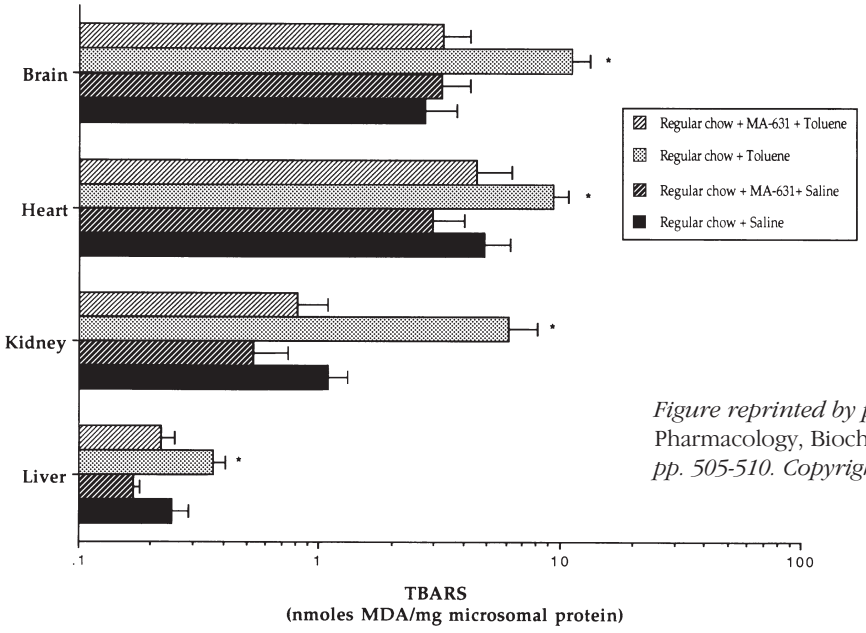


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FIG. 3. Effect of in vivo pretreatment with MA-631 on toluene-induced microsomal lipid peroxidation. Animals were fed regular chow or regular chow supplemented with 2% MA-631 (w:w) for three weeks, then injected IP with toluene or a comparable volume of normal saline. Two hours after injection all animals were sacrificed and microsomal lipid peroxidation was assessed by measuring TBARS. Values are means ± SDs, $n = 6$. *Regular chow + toluene is significantly higher ($p < 0.05$) than regular chow supplemented with 2% (w : w) MA-631 + toluene.

Study 2 **Research Highlights**

An MA-631-supplemented diet pre-fed to rats for 3 weeks completely inhibited the in vivo microsomal lipid peroxidation induced by toluene in rat brain, kidney, liver, and heart.

3. Title

Effect of Herbal Mixture Student Rasayana on Lipoxygenase Activity and Lipid Peroxidation

Publication

Free Radical Biology and Medicine, Vol. 18, No. 4, pp. 687-697, 1995.

Authors

Hari M. Sharma, Atef N. Hanna, Ellen M. Kauffman, and Howard A.I. Newman.

Conducted at

Department of Pathology, College of Medicine, The Ohio State University, Columbus, OH

Summary

Student Rasayana (SR) is an herbal mixture derived from the comprehensive system of natural health care known as Maharishi Ayur-Veda. SR has been reported to increase intelligence in children. This study was undertaken to evaluate the hypothesis that SR improves brain functioning by protecting the brain from free radical damage and/or increasing lipoxygenase activity associated with long-term potentiation (a process associated with memory). The in vivo portion of the study involved feeding rats a 2% (w:w) SR-supplemented diet for three weeks, then challenging their system with an intraperitoneal injection of toluene. The results showed that SR completely inhibited in vivo toluene-induced microsomal lipid peroxidation in rat brain microsomes ($p<0.05$).

For more information on this study, see Antioxidant Research and Research on Anti-Aging, Neurophysiology and Intelligence.

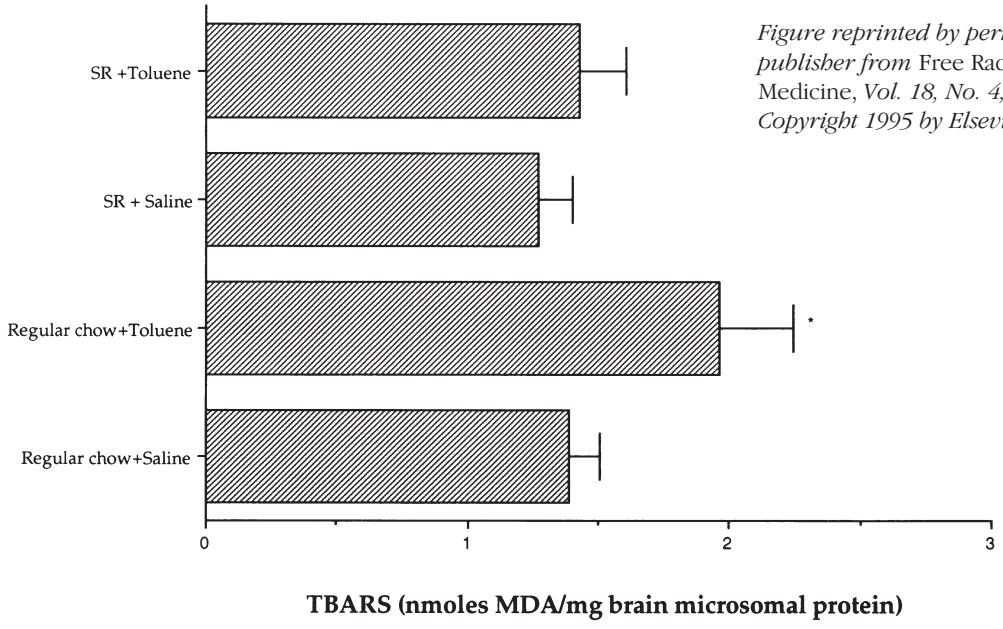


Fig. 5. Effect of in vivo pretreatment with SR on toluene-induced brain microsomal lipid peroxidation. Animals were fed regular chow or regular chow supplemented with 2% (w:w) SR for 3 weeks, then injected intraperitoneally with toluene or a comparable volume of normal saline. Two hours after injection, all animals were sacrificed, and microsomal lipid peroxidation was assessed by measuring TBARS. Values are mean ± SD, $n = 10$. *Regular chow + toluene is significantly higher ($p < 0.05$) than regular chow supplemented with 2% (w:w) SR + toluene.

Study 3 **Research Highlights**

A 2% Student Rasayana (SR)-supplemented diet pre-fed to rats for three weeks completely inhibited in vivo toluene-induced microsomal lipid peroxidation in rat brain microsomes.

Antioxidant Research

1. Title

Inhibitory Effects of Maharishi-4 [MAK-4] and Maharishi-5 [MAK-5] on Microsomal Lipid Peroxidation

Publication

Pharmacology, Biochemistry and Behavior, Vol. 39, No. 3, pp. 649-652, 1991.

Authors

Chandradhar Dwivedi,* Hari M. Sharma,** Stacy Dobrowski,* and Ferzaan N. Engineer.*

Conducted at

* College of Pharmacy, South Dakota State University, Brookings, SD
**College of Medicine, The Ohio State University, Columbus, OH

Summary

The effects of Maharishi-4 (MAK-4) and Maharishi-5 (MAK-5) on microsomal lipid peroxidation were examined in vitro. Rat liver microsomes were incubated with an NADPH-generating system or with sodium ascorbate and an ADP-iron complex to stimulate enzymatic or nonenzymatic lipid peroxidation, respectively. Alcoholic or aqueous extracts of MAK-4 or MAK-5, when added to these incubation systems, inhibited hepatic microsomal lipid peroxidation in a concentration-dependent manner. The aqueous extract of MAK-4 was the most effective antiperoxidant in these systems. A 10% (w/v) aqueous extract of MAK-4 inhibited ascorbate or NADPH-induced lipid peroxidation by approximately 50% when added at volumes of 8 microliters and 3.5 microliters, respectively, to the incubation mixtures (total incubation volume, 2 mL). These findings suggest that MAK-4 and MAK-5, by virtue of their antioxidant properties, may be useful in the treatment of free radical-linked drug toxicities and disease states.

Study 1 **Research Highlights**

Alcoholic or aqueous extracts of MAK-4 or MAK-5, when added to rat liver microsomes incubated with a system to stimulate lipid peroxidation, inhibited hepatic microsomal lipid peroxidation in a concentration-dependent manner. These findings suggest that MAK-4 and MAK-5, by virtue of their antioxidant properties, may be useful in the treatment of free radical-linked drug toxicities and disease states.

2. Title

Effect of Maharishi 4 [MAK-4] and Maharishi 5 [MAK-5] on Inflammatory Mediators—With Special Reference to Their Free Radical Scavenging Effect

Publication

Indian Journal of Clinical Practice, Vol. 1, No. 8, pp. 23-27, January 1991.

Author

Yukie Niwa.

Conducted at

Niwa Institute for Immunology, Japan

Summary

Maharishi 4 (MAK-4) and Maharishi 5 (MAK-5) were investigated for their effects on human neutrophil chemotaxis, phagocytosis, reactive oxygen species (ROS) generation, and lymphocyte response to mitogens. The effect on ROS generated in a xanthine-xanthine oxidase system was also tested. Chemotaxis was significantly inhibited in the presence of MAK-4 and phagocytosis was slightly decreased in the presence of both

MAK-4 and MAK-5. MAK-4 and MAK-5 markedly decreased superoxide, hydrogen peroxide, and hydroxyl radicals, generated both in the neutrophil and xanthine-xanthine oxidase systems. These two herbal mixtures also significantly reduced lymphocyte blastogenesis stimulated by the mitogens phytohemagglutinin, concanavalin A, and pokeweed mitogen. This study suggests that the empirical effectiveness of these two natural products in a variety of diseases is due to their suppressive effect on inflammatory mediators, especially on potent ROS.

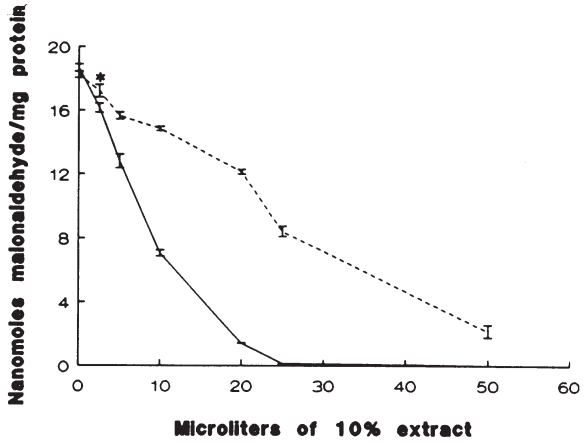


FIG. 1. Effect of M-4 (10% extract) on ascorbate-induced hepatic microsomal lipid peroxidation. The aqueous extract (—) or alcoholic extract (---) was added to the incubation mixture (total incubation volume = 2 ml) described in the Method section. Malonaldehyde values at each point represent the mean ± SD of 3–5 determinations. Values that are not significantly different ($p<0.05$) from the corresponding control value are marked with a * symbol.

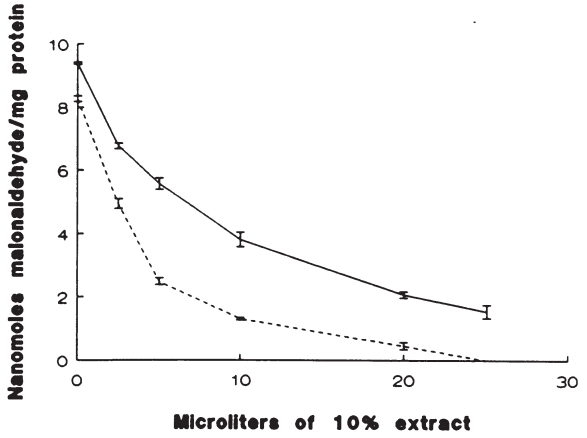


FIG. 4 Effect of M-5 (10% extract) on NADPH-stimulated hepatic microsomal lipid peroxidation. The aqueous extract (—) or alcoholic extract (---) was added to the incubation mixture (total incubation volume = 2 ml) described in the Method section. Malonaldehyde values at each point represent the mean ± SD of 3–5 determinations. Values that are not significantly different ($p<0.05$) from the corresponding control value are marked with a * symbol.

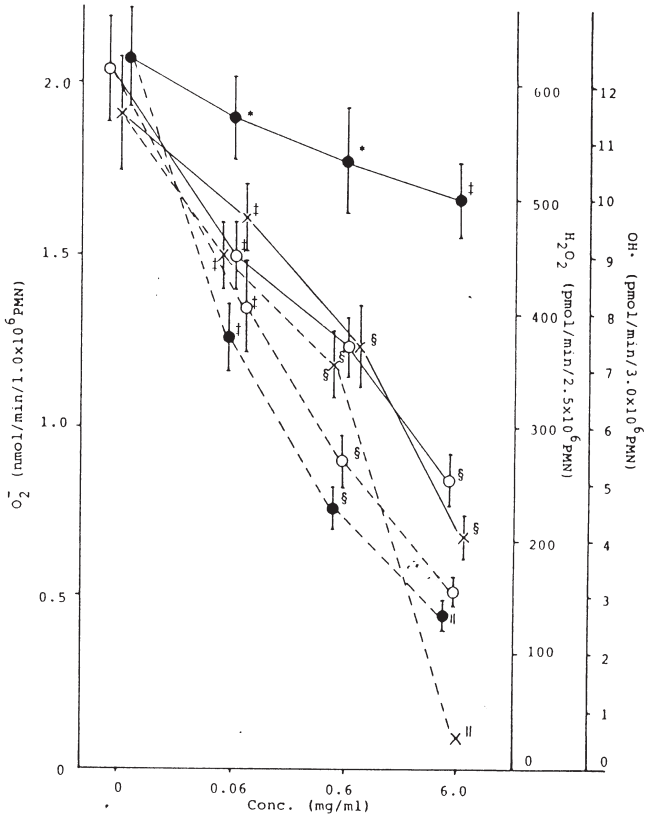


FIG. 2. Effect of MAK-5 on ROS generated by human neutrophils and in xanthine-xanthine oxidase system.
Closed circle (●) denotes O_2 (superoxide);
open circle (O) H_2O_2 (hydrogen peroxide);
and cross symbol (X) OH (hydroxy radical) levels.
Solid line (——) denotes each ROS generated by neurophils, and dashed line (------) in xanthine xanthine oxidase system. PMN denotes polymorphonuclear leukocytes.

*P < 0.05 vs. control, ‡P<0.01, § <0.001, ||P<0.0001.

Study 2 **Research Highlights**
The empirical effectiveness of MAK-4 and MAK-5 in a variety of diseases may be due to their suppressive effect on inflammatory mediators, especially on potent reactive oxygen species (ROS).

3. Title

Inhibition of Human Low-Density Lipoprotein Oxidation In Vitro by Maharishi Ayur-Veda Herbal Mixtures [MAK-4, MAK-5, MA-631, and Maharishi Coffee Substitute]

Publication

Pharmacology, Biochemistry and Behavior, Vol. 43, pp. 1175-1182, 1992.

Authors

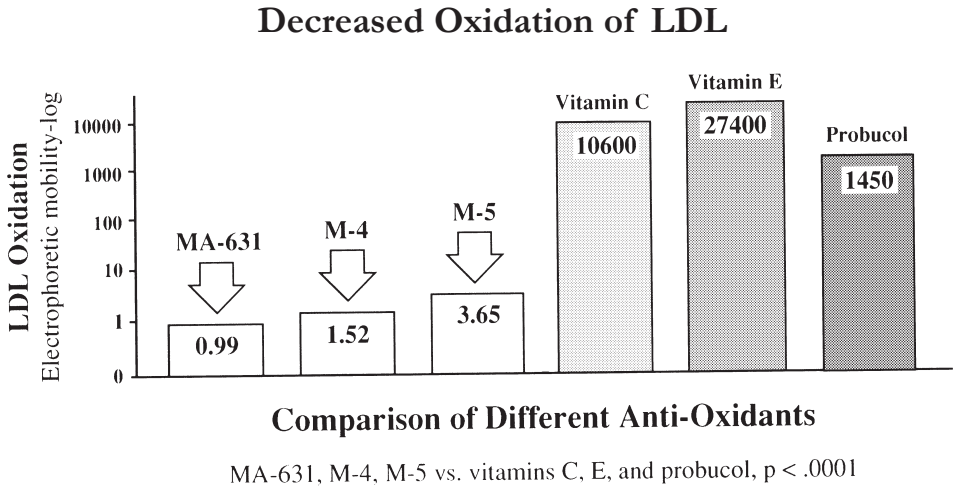
Hari M. Sharma, Atef N. Hanna, Ellen M. Kauffman, and Howard A.I. Newman.

Conducted at

Department of Pathology, College of Medicine, The Ohio State University, Columbus, OH 43210

Summary

This study examined the effect of the Maharishi Ayur-Veda herbal mixtures (MAHMs) MAK-4, MAK-5, MA-631, and Maharishi Coffee Substitute (MCS) on low-density lipoprotein (LDL) oxidation, and compared the potency of these mixtures to ascorbic acid (vitamin C), alpha-tocopherol (vitamin E), and the drug probucol. LDL was incubated in 95% air and 5% CO_2, with or without 3 micromolar Cu^{+2}, in the presence or absence of alcoholic or aqueous extracts of MAHMs, for 6 or 24 hours. In a separate experiment, LDL was incubated as above except the MAHM extracts were added at 0, 1.5, and 3.5 hours after incubation started, to assess their effect on the initiation and propagation of LDL oxidation. The results demonstrate that MAHMs caused concentration-dependent inhibition of LDL oxidation as assessed by thiobarbituric acid-reactive substances (TBARS) and electrophoretic mobility. Both the aqueous and alcoholic extracts of the MAHMs showed more antioxidant potency in preventing LDL oxidation than ascorbic acid, alpha-tocopherol, or probucol. The alcoholic extracts of the MAHMs were at least 1000 times more potent than ascorbic acid, alpha-tocopherol, and probucol after the 6-hour incubation. The alcoholic extracts of the MAHMs showed an even larger magnitude of difference after the 24-hour incubation. Also, the MAHMs inhibited both the initiation and propagation of cupric ion-catalyzed LDL oxidation.



Three Maharishi Ayur-Veda herbal preparations—MA-631, MAK-4 and MAK-5—were much more effective in preventing LDL oxidation than vitamin C and E, and the drug probucol (which are known to be powerful anti-oxidant). LDL oxidation plays a crucial role in the pathology of coronary heart disease. Antioxidant substances help to prevent heart disease by inhibiting oxidation of LDL and other fats.

(continued)

TABLE 1

COMPARISON OF IC_{50} (ng/ml) OF DIFFERENT ANTIOXIDANTS ON LDL OXIDATION AFTER 6-h INCUBATION

Agent	TBARS*	Electrophoretic Mobility*
M-4 aqueous	49.0 ± 7.37	48.4 ± 6.79
M-4 alcoholic	0.708 ± 0.222	1.03 ± 0.145
M-5 aqueous	163 ± 53.7	70.4 ± 14.7
M-5 alcoholic	0.132 ± 0.033	0.72 ± 0.31
MA-631 aqueous	10.2 ± 5.51	9.33 ± 1.69
MA-631 alcoholic	0.152 ± 0.055	1.20 ± 0.488
MCS aqueous	11.7 ± 2.16	–
MCS alcoholic	0.132 ± 0.103	0.967 ± 0.737
Ascorbic acid	$4.00 \pm 0.613 \times 10^3$	$10.5 \pm 1.49 \times 10^3$
α-Tocopherol	$19.6 \pm 3.90 \times 10^3$	$26.0 \pm 4.91 \times 10^3$
Probucol	$1.36 \pm 0.658 \times 10^3$	$2.02 \pm 0.089 \times 10^3$

LDL (0.2 mg) was incubated in 95% air and 5% CO_2, with or without 3 μM Cu^{+2}, in the presence or absence of antioxidant agents for 6 h. Values are mean ± SD ($n = 3$).

*M-4, M-5, MA-631, MCS vs. ascorbic acid, α-Tocopherol, and probucol are significantly different ($p < 0.0001$).

TABLE 2

COMPARISON OF IC_{50} (ng/ml) OF DIFFERENT ANTIOXIDANTS ON LDL OXIDATION AFTER 24-h INCUBATION

Agent	TBARS*	Electrophoretic Mobility*
M-4 aqueous	102 ± 11.2	124 ± 12.6
M-4 alcoholic	0.848 ± 0.387	1.52 ± 0.321
M-5 aqueous	158 ± 70.9	335 ± 55.7
M-5 alcoholic	0.235 ± 0.221	3.653 ± 0.103†
MA-631 aqueous	14.3 ± 5.15	37.3 ± 5.51
MA-631 alcoholic	0.163 ± 0.071	0.988 ± 0.164
MCS aqueous	37.5 ± 8.16	59.2 ± 9.84
MCS alcoholic	0.113 ± 0.028	0.398 ± 0.103
Ascorbic acid	$8.27 \pm 0.678 \times 10^3$	$10.6 \pm 1.70 \times 10^3$
α-Tocopherol	$23.2 \pm 0.924 \times 10^3$	$27.4 \pm 1.46 \times 10^3$
Probucol	453 ± 42.1	$1.45 \pm 0.576 \times 10^3$

Incubation conditions are the same as in Table 1 except incubation was carried out for 24 h. Values are mean ± SD ($n = 3$).

*M-4, M-5, MA-631, MCS vs. ascorbic acid, α-tocopherol, and probucol are significantly different ($p < 0.0001$).

†$n = 2$.

Study 3 **Research Highlights**

Both aqueous and alcoholic extracts of MAK-4, MAK-5, MA-631 and Maharishi Coffee Substitute showed more antioxidant potency in preventing LDL oxidation than ascorbic acid, alpha-tocopherol, or probucol. The alcoholic extracts of MAK-4, MAK-5, and MA-631 were at least 1,000 times more potent than the comparison antioxidants.

4. **Title**

In Vitro and In Vivo Inhibition of Microsomal Lipid Peroxidation by MA-631

Publication

Pharmacology, Biochemistry and Behavior, Vol. 48, No. 2, pp. 505-510, 1994.

Authors

Atef N. Hanna, Hari M. Sharma, Ellen M. Kauffman, and Howard A. I. Newman.

Conducted at

Department of Pathology, College of Medicine, The Ohio State University, Columbus, OH 43210

Summary

Excess free radicals are linked to many diseases, including aging, atherosclerosis, and cancer. MA-631 (a complex herbal mixture) has been shown to inhibit human low-density lipoprotein (LDL) oxidation in vitro. In this study, further evaluation was undertaken on the in vivo and in vitro antioxidant activity of MA-631. Both the alcoholic and aqueous extracts of MA-631 inhibited enzymatic- and nonenzymatic-induced rat liver microsomal lipid peroxidation in a concentration-dependent manner ($p<0.05$). The thiobarbituric acid-reactive substances (TBARS) values (nmoles malondialdehyde (MDA)/mg microsomal protein) were 1.43 +/- 0.18 for microsomes alone (baseline for enzymatic system), 19.63 +/- 2.50 for microsomes + reduced nicotinamide adenine dinucleotide phosphate (NADPH) (oxidation without inhibitor), 9.89 +/- 1.41 for heated microsomes (baseline for nonenzymatic system), and 27.15 +/- 0.08 for microsomes + ascorbate (oxidation without inhibitor). The concentrations (microgram/2 mL) of MA-631 which produced 50% inhibition (IC_{50}) of enzymatic- and nonenzymatic-induced lipid peroxidation were 15.2 +/- 2.0 and 17.0 +/- 2.6, respectively, for the aqueous extract, and 4.3

+/- 0.8 and 6.4 +/- 1.2, respectively, for the alcoholic extract. These results imply that MA-631 may be useful in the prevention of free radical-linked diseases.

See Research on Reduction of Chemical Toxicity for more information on this study.

Study 4 **Research Highlights**
Both alcoholic and aqueous extracts of MA-631 inhibited rat liver microsomal lipid peroxidation in a concentration-dependent manner. The results suggest that MA-631 may be useful in the prevention of free-radical-linked diseases.

5. Title
Protective Effects of MAK-4 and MAK-5 on Adriamycin-Induced Microsomal Lipid Peroxidation and Mortality

Publication
Biochemical Archives, Vol. 8, pp. 267-272, 1992.

Authors
Ferzaan N. Engineer,* Hari M. Sharma,** and Chandradhar Dwivedi.*

Conducted at
* College of Pharmacy, South Dakota State University, Brookings, SD
**College of Medicine, The Ohio State University, Columbus, OH

Summary
The clinical usefulness of the chemotherapeutic agent Adriamycin is compromised by dose-dependent and potentially lethal cardiac toxic effects. The cardiotoxicity of Adriamycin may be linked with free radical-mediated peroxidation of microsomal lipids. This study examined the effects of MAK-4 and MAK-5, herbal food supplements, on Adriamycin-induced lipid peroxidation and toxicity. Rat liver microsomes were incubated with an NADPH-generating system to stimulate lipid peroxidation in the presence or absence of Adriamycin. Alcoholic or aqueous extracts of MAK-4 and MAK-5, when added to these incubation systems, inhibited hepatic microsomal lipid peroxidation in a concentration-dependent manner. The 10% ethanolic or aqueous extract of MAK-4 was a highly effective inhibitor of lipid peroxidation. The ethanolic extract (10%) of MAK-5 also inhibited lipid peroxidation. However, the 10% aqueous extract of MAK-5 did not exhibit antiperoxidant properties under these experimental conditions.

See Cancer Research for more information on this study.

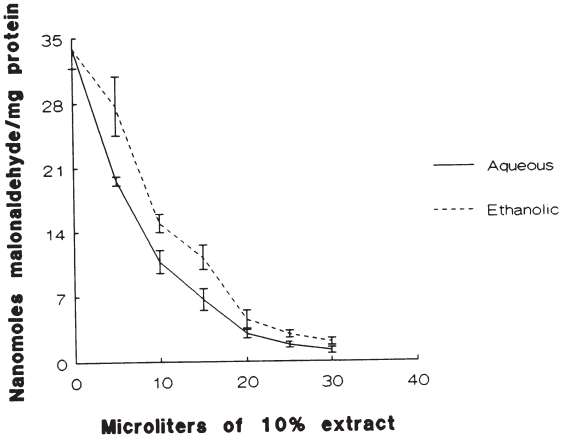


Figure 1
Effects of M-4 (10% extract) on Adriamycin-stimulated hepatic microsomal lipid peroxidation. Malonaldehyde values at each point represent the mean ± SD of 3-6 determinations. The value for control incubations in the absence of Adriamycin was 22.75±3.8 nanomoles malonaldehyde/mg protein.

Study 5 **Research Highlights**
Cardiotoxicity of the chemotherapeutic agent Adriamycin may be linked with free radical-mediated peroxidation of microsomal lipids. Alcoholic or aqueous extracts of MAK-4 and MAK-5, when added to lipid peroxidation incubation systems, inhibited hepatic microsomal lipid peroxidation in a concentration-dependent manner.

6. Title

In Vivo Effect of Herbal Mixture MAK-4 on Antioxidant Capacity of Brain Microsomes

Publication

Biochemical Archives, Vol. 12, pp. 181-186, 1996.

Authors

Hari M. Sharma, Jae Y. Lee, Ellen M. Kauffman, and Atef N. Hanna.

Conducted at

Department of Pathology, College of Medicine, The Ohio State University, Columbus, OH 43210

Summary

There is increasing evidence that free radicals are linked to neurological disorders and aging. The herbal mixture Maharishi Amrit Kalash-4 (MAK-4) has antioxidant properties, as assessed by inhibition of low-density lipoprotein oxidation in vivo and in vitro. This study examined the in vivo effect of MAK-4 on lipid peroxidation and antioxidant protection capacity of the brain of Watanabe Heritable Hyperlipidemic (WHHL) rabbits. A group of 5 rabbits (controls) were fed normal rabbit chow, and a group of 6 rabbits were fed normal chow supplemented with 6% MAK-4 (w:w) for 6 months. Brain microsomes were then prepared and incubated in the presence or absence of either an enzymatic or nonenzymatic system for inducing lipid peroxidation; in the absence of either system, air-induced lipid peroxidation was measured. Lipid peroxidation was assessed by measuring thiobarbituric acid-reactive substances (TBARS). The baseline level of TBARS (nmoles malondialdehyde/mg microsomal protein) was significantly lower ($p<0.05$) in the rabbits fed MAK-4 (1.18 +/- 0.07 vs. 1.51 +/- 0.25 for controls). Also, the MAK-4 group showed significantly lower TBARS ($p<0.05$) after air-, enzymatic-, and nonenzymatic-induced lipid peroxidation (1.29 +/- 0.21, 1.27 +/- 0.16, and 2.91 +/- 0.79, respectively), as compared to controls (1.92 +/- 0.45, 2.28 +/- 0.26, and 12.85 +/- 0.61, respectively). These results indicate MAK-4 may yield increased antioxidant protection in the brain, and may therefore be useful in preventing or treating free radical-induced neurological disorders.

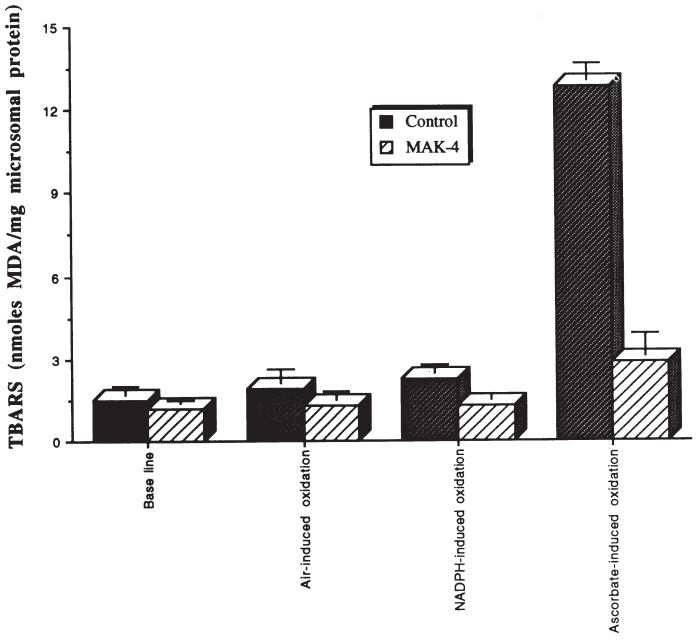


Figure 1

The effect of MAK-4 on resistance of brain microsomes to oxidation. WHHL rabbits were fed regular rabbit chow + 6% MAK-4 (MAK-4 group) or regular chow alone (control group) for 6 months. Brain microsomes were prepared by ultracentrifugation. The microsomes were incubated alone (air-induced oxidation), or with an NADPH-generating system, or with an ascorbate-Fe^{+3} system. The degree of oxidation was assessed by measuring TBARS before incubation (baseline) or after incubation with the various oxidants. Values are mean ± S.E.

Study 6 **Research Highlights**

As studied in Watanabe Heritable Hyperlipidemic rabbits, MAK-4 may yield increased antioxidant protection in the brain, and may therefore be useful in preventing or treating free radical-induced neurological disorders.

7. Title

Antioxidant Properties of Two Ayurvedic Herbal Preparations [MAK-4 and MAK-5]

Publication

Biochemical Archives, Vol. 10, pp. 25-31, 1994.

Authors

Stephen C. Bondy, Tina M. Hernandez, and Cara Mattia.

Conducted at

Department of Community and Environmental Medicine, University of California (Irvine), Irvine, CA 92717

Summary

Two herbal preparations (MAK-4 and MAK-5) constituted of mixtures of several plants have been used over a long period of time by practitioners of Ayurvedic medicine. In view of several reports on their health-related utility, this investigation was undertaken to study their properties in biological systems. Results of this study showed that ethanol and aqueous extracts of these preparations were able to quench generation of reactive oxygen species in vitro within an isolated cerebrocortical fraction enriched in mitochondria and nerve endings (synaptosomes). Both the ethanol and aqueous extracts of MAK-4 and MAK-5 exhibited potent antioxidant activity. The greatest effect was seen with the ethanol extracts of these herbal mixtures, and the most potent inhibition was found in ethanol-soluble materials derived from the MAK-5 product. The ability of MAK-5 extracts to modulate chemically-induced oxidative stress was also examined in intact animals. The excess production of reactive oxygen species observed within the cerebellar mitochondrial fraction after exposure of rats to toluene, was prevented by pretreatment with MAK-5. This effect was not apparent when the ethanol and aqueous extracts of the preparation were tested separately. However, the ethanol extract from MAK-5 alone was able to inhibit the toluene-induced elevation of oxidative species within a mitochondrial fraction derived from the kidney. The results suggest that these herbally-derived mixtures possess distinctive qualities which may be of utility in the design of preventive or therapeutic approaches relating to the mitigation of excess oxidative events. See Research on Reduction of Chemical Toxicity for more information on this study.

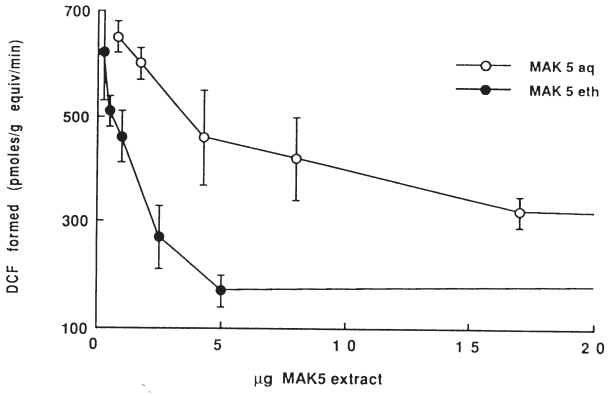


FIGURE 1

Effect of aqueous and ethanol extracts of MAK-5 on rates of synaptosomal oxygen radical formation. Data points are derived from 4-8 independent assays ± standard error

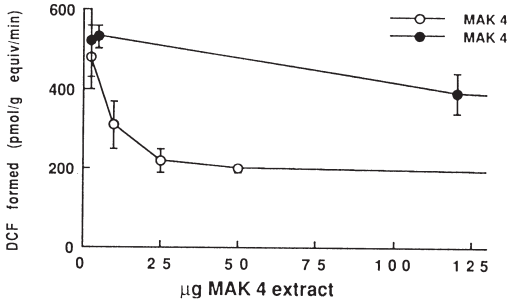


FIGURE 2

Effects of aqueous and ethanol extracts of MAK-4 on rates of synaptosomal oxygen formation. Data are derived from 4-9 individual determinations ± standard error.

Study 7 **Research Highlights**

Ethanol and aqueous extracts of MAK-4 and MAK-5 were able to quench generation of reactive oxygen species in vitro within an isolated cerebrocortical fraction enriched in mitochondria and nerve endings. Thus, these herbally-derived mixtures possess distinctive qualities, which may be of utility in the design of preventive or therapeutic approaches related to the mitigation of excess oxidative events.

8. Title

Effect of Herbal Mixtures MAK-4 and MAK-5 on Susceptibility of Human LDL to Oxidation

Publication

Complementary Medicine International, Vol. 3, No. 3, pp. 28-36, May/June 1996.

Authors

Atef N. Hanna, PhD,* Vidya Sundaram, MD,** James M. Falko, MD,** Ralph E. Stephens, PhD,* and Hari M. Sharma, MD, FRCPC.*

Conducted at

*Department of Pathology and **Department of Internal Medicine, College of Medicine, The Ohio State University, Columbus, OH 43210

Summary

Oxidation of low-density lipoprotein (LDL) plays a central role in the pathogenesis of atherosclerosis. This study investigated the in vivo antioxidant activity of MAK-4 and MAK-5 in a clinical setting, and investigated the in vitro antioxidant properties of MAK-4. Both the aqueous and alcoholic extracts of MAK-4 inhibited endothelial cell (EC)- and soybean lipoxygenase (SLP)-induced LDL oxidation in a concentration-dependent manner. The agent concentrations (microgram/mL) which inhibited 50% (IC_{50}) of EC- and SLP-induced LDL oxidation, respectively, were 150.0 +/- 10.0 and 488.3 +/- 41.9 for the aqueous extract, and 69.3 +/- 8.1 and 128.3 +/- 18.9 for the alcoholic extract. In vitro pretreatment of LDL with MAK-4 increased the resistance of LDL to Cu^{+2}-catalyzed LDL oxidation. Both the aqueous and alcoholic extracts inhibited free radical generation in a concentration-dependent manner. The IC_{50} was 16.35 +/- 4.27 for the aqueous extract, and 3.64 +/- 1.24 for the alcoholic extract; addition of both extracts showed a synergistic interaction. In hyperlipidemic patients, MAK-4 and MAK-5 increased resistance of LDL to oxidation by Cu^{+2} and EC. These results suggest that MAK-4 and MAK-5 protect LDL from oxidation and may be useful in the prevention and treatment of atherosclerosis.

See Cardiovascular Research for more information on this study.

Study 8 **Research Highlights**

MAK-4 and MAK-5 increased resistance of LDL to oxidation by Cu^{+2} and EC in hyperlipidemic patients. These results suggest that MAK-4 and MAK-5 protect LDL from oxidation and may be useful in the prevention and treatment of atherosclerosis.

9. Title

Effect of Herbal Mixture Student Rasayana on Lipoxygenase Activity and Lipid Peroxidation

Publication

Free Radical Biology and Medicine, Vol. 18, No. 4, pp. 687-697, 1995.

Authors

Hari M. Sharma, Atef N. Hanna, Ellen M. Kauffman, and Howard A.I. Newman.

Conducted at

Department of Pathology, College of Medicine, The Ohio State University, Columbus, OH

Summary

Brain cellular functions are affected by free radicals. Arachidonic acid and its 12-lipoxygenase metabolites have been proposed as important in enhancing long-term potentiation associated with learning. It has been reported that Student Rasayana (SR), an herbal mixture, improves brain functions. This study evaluated the antioxidant capacity of SR and its effect on lipoxygenase activity. Both the alcoholic and aqueous extracts of SR inhibited enzymatic- and nonenzymatic-induced microsomal lipid peroxidation in a concentration-dependent manner ($p<0.05$). The agent concentrations (microgram/mL) that produced 50% inhibition (IC_{50}) of enzymatic- and nonenzymatic-induced microsomal lipid peroxidation, respectively, were 99.1 +/- 3.9 and 1992.0 +/- 122.7 for the aqueous extract, and 17.7 +/- 0.9 and 646.7 +/- 79.7 for the alcoholic extract. The aqueous extract inhibited soyabean lipoxygenase (SLP)-induced LDL oxidation in a concentration-dependent manner (IC_{50}: 515.5 +/- 11.5) ($p<0.05$), whereas the alcoholic extract enhanced SLP-induced LDL oxidation. Simultaneous addition of the aqueous and alcoholic extracts inhibited SLP-induced LDL oxidation ($p<0.05$). The alcoholic extract (but not the aqueous extract) enhanced the ability of SLP to induce oxidation of linoleic acid. These results suggest SR improves brain functions through scavenging free radicals as well as increasing the second messenger for long-term potentiation.

See Research on Reduction of Chemical Toxicity and Research on Anti-Aging, Neurophysiology and Intelligence for more information on this study.

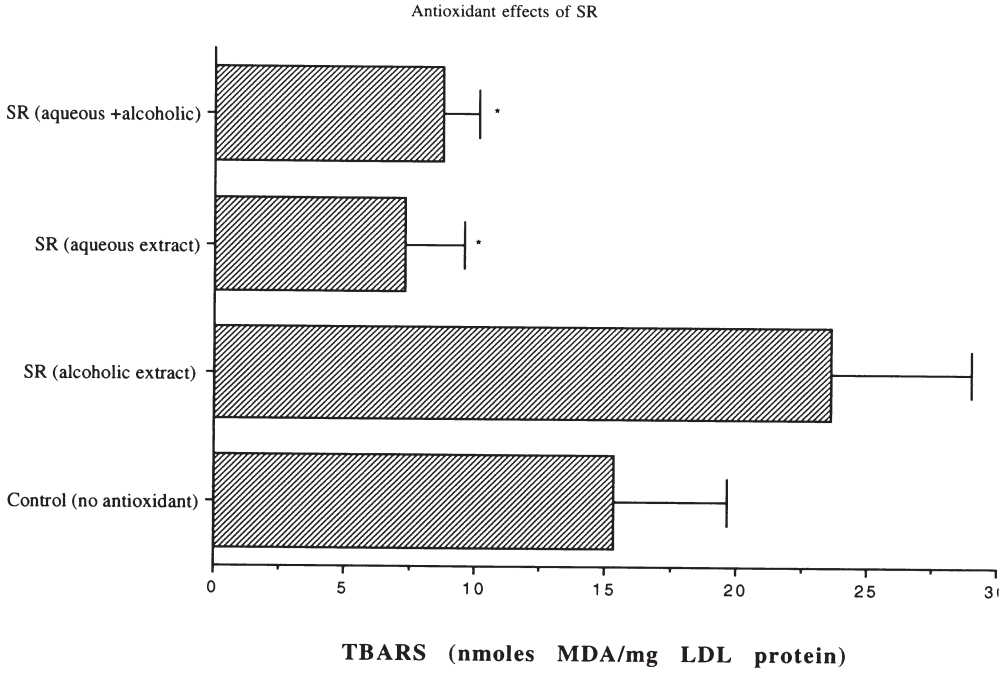


Fig. 1. Effect of simultaneous addition of alcoholic and aqueous extracts of SR on lipoxygenase-induced LDL oxidation. LDL was incubated with or without SLP and phospholipase A_2, in the presence or absence of the alcoholic extract (52 μg) and/or the aqueous extract (640 μg) of SR, at 37°C for 24 h. The degree of LDL oxidation was assessed by measuring TBARS. Values are mean ± *SD*, $n = 3$. *Significantly lower ($p < 0.05$) than the control or the incubation mixture containing only the alcoholic extract of SR.

Study 9 **Research Highlights**

Student Rasayana may improve brain functions through scavenging free radicals as well as increasing the second messenger for long-term potentiation.

10. Title

Inhibition of Low-Density Lipoprotein Oxidation by Oral Herbal Mixtures Maharishi Amrit Kalash-4 (MAK-4) and Maharishi Amrit Kalash-5 (MAK-5) in Hyperlipidemic Patients

Publication

The American Journal of the Medical Sciences, Vol. 314, No. 5, pp. 303-310, 1997.

Authors

Vidya Sundaram, M.D.,* Atef N. Hanna, Ph.D.,** Gary P. Lubow, M.D.,** Lata Koneru, M.D.,† James M. Falko, M.D.,* and Hari M. Sharma, M.D.**

Conducted at

*Department of Internal Medicine and **Department of Pathology, College of Medicine, The Ohio State University, Columbus, OH
†Department of Internal Medicine, Riverside Methodist Hospital, Columbus, OH.

Summary

Low-density lipoprotein (LDL) oxidation is central to the pathogenesis of atherosclerosis. This study evaluated the antioxidant activity of MAK-4 and MAK-5 in vivo. Ten hyperlipidemic patients prescribed stable hypolipidemic therapy were treated with MAK-4 and MAK-5 for 18 weeks. Plasma lipoprotein, plasma lipid peroxide, and LDL oxidation studies were performed every 6 weeks. Apolipoprotein A, apolipoprotein B, and lipoprotein (a) levels were measured at baseline and 18 weeks. After 12 weeks of treatment with MAK-4 and MAK-5, a time-dependent increase in the lag phase and delay in the propagation phase of oxidation of LDL by Cu^{+2} and endothelial cells was seen. Lag phases at baseline and after 6, 12, and 18 weeks of MAK-4 and MAK-5 ingestion were 6.66 hours ± 0.19 (mean ± standard error of mean), 6.77 hours ± 0.31, 7.22 hours ± 0.24, and 18.00 hours ± 0.73, respectively, for Cu^{+2}-catalyzed LDL oxidation. Lag phases were 14.89 hours ± 0.77, 13.33 hours ± 0.50, 20.22 hours ± 0.76, and 20.00 hours ± 0.79, respectively, for endothelial cell-induced LDL oxidation. The levels of plasma lipid peroxide did not change significantly. No significant changes were seen in the plasma lipoproteins and the levels of apolipoprotein A, apolipoprotein B, and lipoprotein (a). The results show that MAK-4 and MAK-5 inhibit LDL oxidation in patients with hyperlipidemia. Therefore, MAK-4 and MAK-5 may be useful in the prevention and treatment of atheroslerosis.

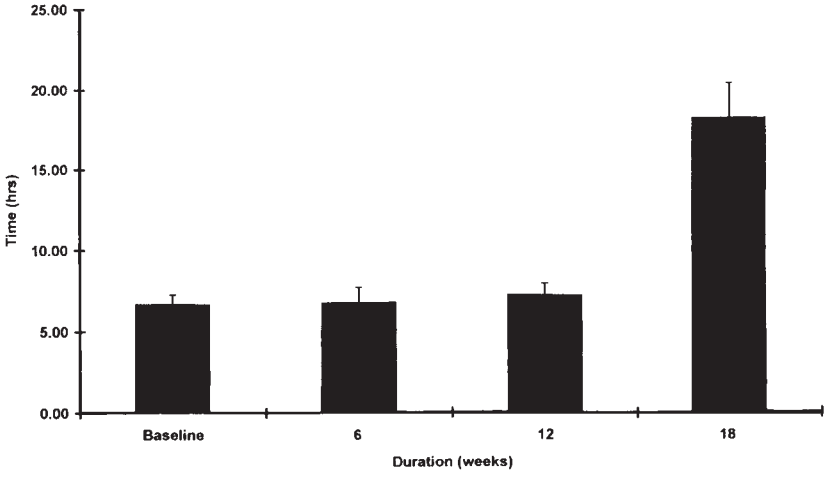


Figure 2. Lag phase (mean ± standard error of mean) of Cu^{+2}-induced low-density lipoprotein oxidation at baseline (0 weeks) and after 6, 12, and 18 weeks of treatment with MAK-4 and MAK-5. *P < 0.05

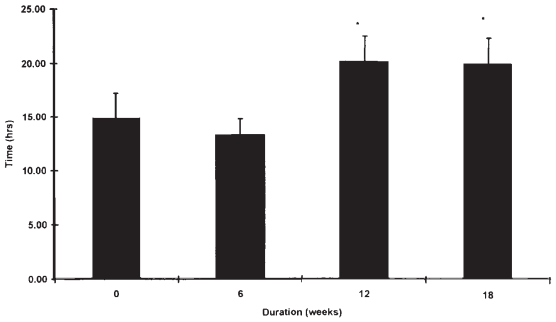


Figure 3. Lag phase (mean ± standard error of mean) of endothelial cell-induced low-density lipoprotein oxidation at baseline (0 weeks) and after 6, 12, and 18 weeks of treatment with MAK-4 and MAK-5. * $P < 0.05$

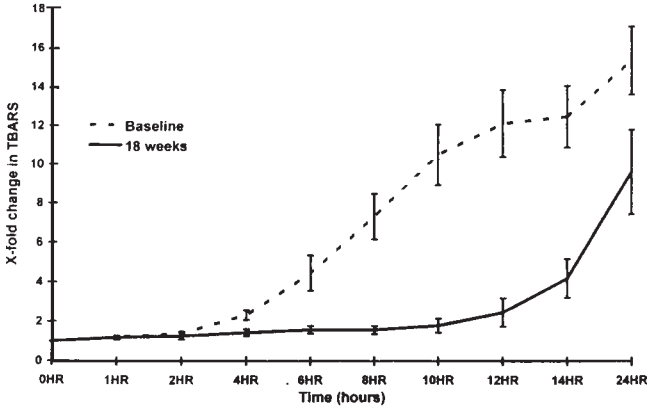


Figure 4. Plot depicting Cu^{+2}-induced low-density lipoprotein oxidation at baseline and after 18 weeks of treatment with MAK-4 and MAK-5. Y-axis represents x-fold change (mean ± standard error of mean) in thiobarbituric acid-reactive substances.

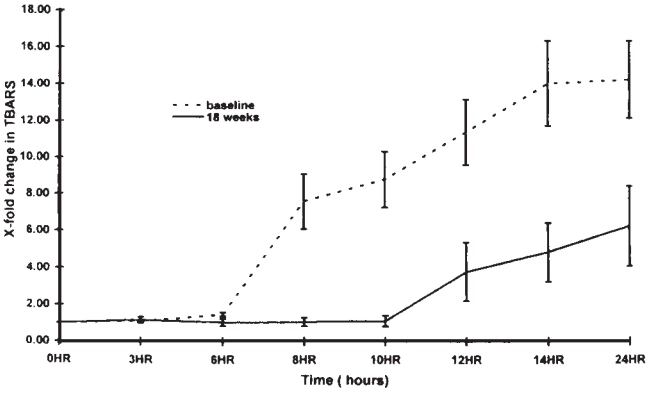


Figure 5. Plot depicting endothelial cell-induced low-density lipoprotein oxidation at baseline and after 18 weeks of treatment with MAK-4 and MAK-5. Y-axis represents x-fold change (mean ± standard error of mean) in thiobarbituric acid-reactive substances.

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Study 10 **Research Highlights**
Ten hyperlipidemic patients were treated with MAK-4 and MAK-5 for 18 weeks. After 12 weeks of treatment, a time-dependent increase in the lag phase and delay in the propagation phase of oxidation of LDL by Cu^{+2} and endothelial cells was seen. Therefore, MAK-4 and MAK-5 may be useful in the prevention and treatment of atherosclerosis.

11. Title

The Antioxidant and Antiatherogenic Effects of MAK-4 in WHHL Rabbits

Publication

Journal of Alternative and Complementary Medicine, Vol. 2, No. 4, pp. 463-478, 1996.

Authors

Jae Y. Lee, PhD, Atef N. Hanna, PhD, John A. Lott, PhD, and Hari M. Sharma, MD, FRCPC.

Conducted at

Department of Pathology, College of Medicine, The Ohio State University, Columbus, OH 43210

Summary

This study tested the effect of MAK-4 on the development of atheroma in WHHL rabbits. Eleven rabbits were divided into two groups: controls (n = 5) and a group fed 6% (w/w) MAK-4 (n = 6). Blood was drawn for biochemical analysis every two months and at necropsy, six months after the special diet was started. The aortas were preserved in formalin. The percentage area of aortic arch covered with visible plaque in the MAK-4 group (22.5 ± 4.2%, mean ± SE) was significantly reduced (p <0.01) compared to the control group (47.6 ± 6.8%, mean ± SE). The MAK-4 group showed a significant decrease (p <0.05) in lipid peroxide, and a significant increase (p <0.05) in glutathione peroxidase and resistance of LDL to endothelial cell-induced and cupric ion-catalyzed oxidation (4.5 h and 5 h lag phase, respectively, for the MAK-4 group; 0 h lag phase for both for the controls). These findings suggest MAK-4 reduces atheroma formation through its antioxidant activity. See Cardiovascular Research for more information on this study.

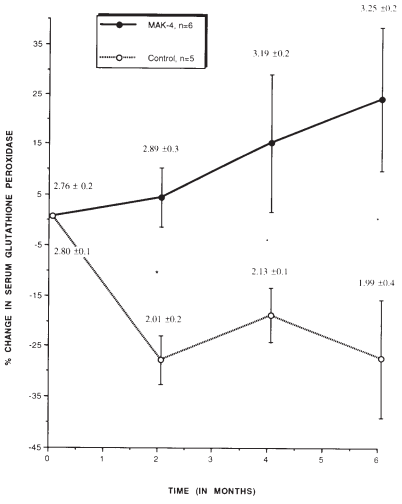

FIG. 3. Effect of MAK-4 on serum glutathione peroxidase activity in WHHL rabbits. Glutathione peroxidase is expressed as U/gm protein. Values are mean ± SE. *p < 0.05

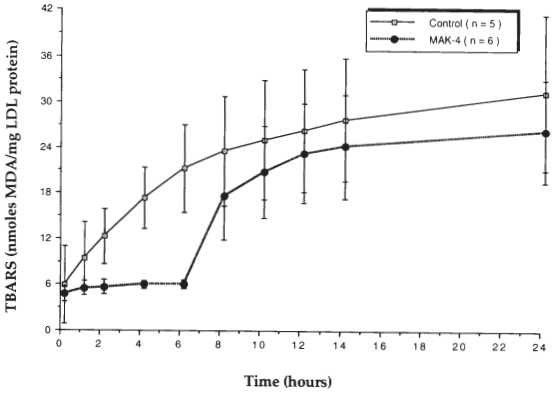

FIG. 4. Effect of MAK-4 on lag phase and propagation phase of cupric ion–catalyzed LDL oxidation at month 6, as assessed by measuring TBARS. LDL (0.2 mg) was incubated with or without 1 μM Cu^{+2} in a humidified environment of 95% air and 5% CO_2 at 37°C for various times. The degree of LDL oxidation was assessed by measuring TBARS. Values are mean ± SE. The concentration of TBARS at 4 h and 6 h in the MAK-4 group is significantly lower (p < 0.05) than the control group.

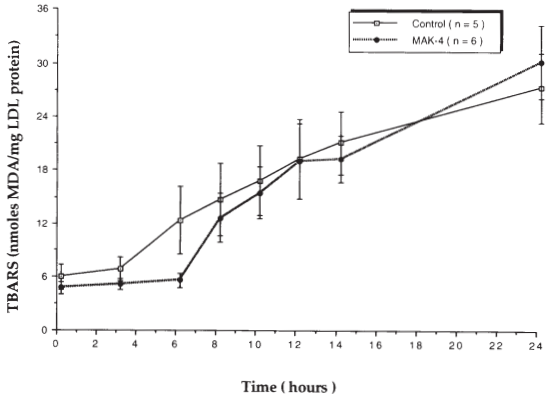

FIG. 5. Effect of MAK-4 on lag phase and propagation phase of endothelial cell–induced LDL oxidation at month 6. LDL (0.2 mg) was incubated with or without endothelial cells in a humidified environment of 95% air and 5% CO_2 at 37°C for various times. The degree of LDL oxidation was assessed by measuring TBARS. Values are mean ± SE.

Study 11 **Research Highlights**

This study conducted with Watanabe Heritable Hyperlipidemic (WHHL) rabbits suggests that MAK-4 reduces atheroma formation through its antioxidant activity. (Atheroma refers to the fatty degeneration or thickening of the walls of the arteries in atherosclerosis.)

12. Title

In Vitro Inhibition of Microsomal Lipid Peroxidation by MA-631, Student Rasayana (SR), Ladies Rasayana (LR), and Maharishi Coffee Substitute (MCS)

Publication

The Pharmacologist, Vol. 34, No. 3, p. 184, 1992 (Abstract).

Authors

H.M. Sharma, A. Hanna, E.M. Kauffman, and H.A.I. Newman.

Conducted at

College of Medicine, The Ohio State University, Columbus, OH 43210

Summary

In this study, the effects of MA-631, SR, LR, and MCS on microsomal lipid peroxidation were examined in vitro. Rat liver microsomes were incubated with a sodium ascorbate and ADP-iron complex or with an NADPH-generating system to stimulate nonenzymatic or enzymatic lipid peroxidation, respectively. Aqueous or alcoholic extracts of MA-631, SR, LR, and MCS, when added to these incubation systems, inhibited hepatic microsomal lipid peroxidation in a dose-dependent manner. The alcoholic extracts were the most effective antiperoxidants in both systems. The alcoholic extract of MCS inhibited ascorbate- or NADPH-induced lipid peroxidation by 56% and 63%, with 12 micrograms and 22.5 micrograms, respectively. These findings suggest that these Maharishi Ayur-Veda food supplements may be useful in the treatment of free radical-induced injury due to their antiperoxidant properties.

Study 12 **Research Highlights**

In vitro aqueous and alcoholic extracts of MA-631, Student Rasayana, Ladies Rasayana, and Maharishi Coffee Substitute demonstrated potent antiperoxidant properties in a dose-dependent manner. Thus, these supplements may be useful in the treatment of free radical-induced injury due to their antiperoxidant properties.

13. Title

Maharishi Amrit Kalash [MAK-4 and MAK-5] Rejuvenates Ageing Central Nervous System's Antioxidant Defense System: An *In Vivo* Study

Publication

Pharmacological Research, Vol. 40, No. 6, pp 497-502, 1999.

Authors

Bhupinder Pal Singh Vohra,* Satya Prakash Sharma,* and Vinod Kumar Kansal.**

Conducted at

* Laboratory of Nutritional Histopathology and Ageing, Department of Zoology, Kurukshetra University, Kurukshetra—136 119, Haryana, India

**Animal Biochemistry Division, National Dairy Research Institute, Karnal, Haryana, India

Summary

The oxygen-free radical involvement in various deteriorative processes and in aging is unquestionably established. In the present study, age-related changes in antioxidant enzyme activity in the different regions of CNS of 10-month and 32-month-old guinea pigs were studied. Maharishi Amrit Kalash has shown promise in inhibiting the *in vitro* and *in vivo* lipid peroxidation. Therefore, in the present study the effect of MAK on the activity of antioxidant enzymes was checked. Our results indicate that the activity of superoxide dismutase and glutathione peroxidase, was found to be reduced $p < 0.05$ in all the regions of CNS studied. The activities of catalase declined significantly only in the cerebral cortex, hypothalamus and the cerebellum, whereas glutathione reductase activity declined in the cerebral cortex and hypothalamus. It is concluded that the age-related decline in the activities of antioxidant enzymes is region-specific as well as enzyme-specific. The endogenous lipid peroxide was found to be increased significantly $p < 0.05$ in the 32-month-old animals, whereas the lipid peroxidation after incubating the tissue homogenate in the air was found to be decreased $p < 0.05$ in the older animals. The results indicate that the accumulation of lipid peroxides takes place with age but the susceptibility of lipid peroxidation decreases in the older animals. The treatment of MAK 500 mg kg^{-1} body wt. for 2 months could augment the activities of antioxidant enzymes $p < 0.05$. The effect of MAK was more pronounced in older than younger animals. It is concluded that the MAK can be used in compensating the decline in the activities of antioxidant enzymes in CNS and thereby it reduces the risks of lipid peroxidation.

Table I
Effect of MAK on the activity of Cu / Zn-superoxide dismutase

Tissue	*Young animals (10 months)*		*Old animals (32 months)*	
	Control	*Treated*	*Control*	*Treated*
Cerebral cortex	26.57 ± 1.02	36.67 ± 3.46*	13.24 ± 2.56**	25.14 ± 1.43*
Hypothalamus	26.56 ± 1.54	40.04 ± 1.56*	13.14 ± 2.37**	24.72 ± 2.96*
Rest of the cerebrum	28.10 ± 1.53	30.98 ± 1.10	18.10 ± 1.10**	24.25 ± 1.09*
Brain-stem	32.52 ± 1.80	41.91 ± 2.37*	16.48 ± 2.65**	30.89 ± 1.13*
Cerebellum	30.93 ± 1.44	40.46 ± 1.51*	15.67 ± 2.37**	24.21 ± 1.47*
Spinal cord	35.41 ± 1.56	41.14 ± 1.20*	19.39 ± 1.40**	30.06 ± 2.12*

Notes. The activity of enzyme is defined as the amount of enzyme required to inhibit 50% reduction of NBT. Values in the table represent enzyme units per milligram of protein. Data are mean ± SEM of five animals. * Values are significantly different from the controls within the same age group $P < 0.05$; ** values are significantly different from young controls $P < 0.05$.

Table II
Effect of MAK on the activity of Mn-superoxide dismutase

Tissue	*Young animals (10 months)*		*Old animals (32 months)*	
	Control	*Treated*	*Control*	*Treated*
Cerebral cortex	18.05 ± 1.38	21.57 ± 1.75	11.76 ± 1.02**	20.41 ± 0.95*
Hypothalamus	19.82 ± 0.95	23.20 ± 1.30	10.59 ± 1.35**	18.26 ± 1.45*
Rest of the cerebrum	21.05 ± 2.67	29.85 ± 1.56*	11.28 ± 1.24**	20.05 ± 1.74*
Brain-stem	22.94 ± 0.76	29.87 ± 1.56*	14.79 ± 1.24**	23.24 ± 1.74*
Cerebellum	23.59 ± 0.79	30.84 ± 1.61*	17.06 ± 1.16**	23.61 ± 1.37*
Spinal cord	24.29 ± 2.37	30.25 ± 2.77	16.94 ± 1.28**	24.49 ± 2.37*

Notes. The activity of enzyme is defined as the amount of enzyme required to inhibit 50% reduction of NBT. Values in the table represent enzyme units mg^{-1} protein. Data are mean ± SEM of five animals. * Values are significantly different from the controls within the same age group $P < 0.05$; ** values are significantly different from young controls $P < 0.05$.

Table III
Effect of MAK on the activity of catalase

Tissue	*Young animals (10 months)*		*Old animals (32 months)*	
	Control	*Treated*	*Control*	*Treated*
Cerebral cortex	42.32 ± 1.54	44.31 ± 1.22	19.54 ± 2.33**	30.74 ± 1.28*
Hypothalamus	36.29 ± 1.63	47.80 ± 1.16*	21.14 ± 1.90**	22.99 ± 1.35
Rest of the cerebrum	61.46 ± 4.54	63.89 ± 2.58	62.37 ± 3.10	68.10 ± 2.97
Brain-stem	46.89 ± 3.74	51.07 ± 1.76	40.82 ± 1.78	46.60 ± 1.78
Cerebellum	79.44 ± 2.00	95.41 ± 3.03*	51.17 ± 3.96**	51.19 ± 3.19
Spinal cord	34.10 ± 2.20	42.66 ± 2.14*	28.60 ± 4.36	34.80 ± 2.27*

Notes. The activity of enzyme is expressed as micromoles of H_2O_2 decomposed per minute per milligram protein. Data are mean ± SEM of five animals. * Values are significantly different from the controls within the same age group $P < 0.05$; ** values are significantly different from young controls $P < 0.05$.

Table IV
Effect of MAK on the activity of glutathione peroxidase

Tissue	*Young animals (10 months)*		*Old animals (32 months)*	
	Control	*Treated*	*Control*	*Treated*
Cerebral cortex	37.78 ± 1.36	43.99 ± 1.50*	21.54 ± 1.39**	32.07 ± 1.87*
Hypothalamus	41.15 ± 2.53	50.46 ± 1.31*	23.87 ± 2.19**	40.25 ± 2.69*
Rest of the cerebrum	38.84 ± 2.85	45.77 ± 2.27	20.77 ± 1.61**	36.14 ± 2.54*
Brain-stem	37.75 ± 1.80	46.19 ± 3.26*	25.61 ± 1.93**	38.48 ± 1.74*
Cerebellum	45.12 ± 1.01	51.17 ± 3.29	27.65 ± 1.61**	43.94 ± 2.94*
Spinal cord	51.29 ± 2.47	59.95 ± 2.30*	30.95 ± 1.64**	49.68 ± 2.39*

Notes. The activity of enzyme is expressed as nanomoles of NADPH oxidised per minute per milligram of protein. Data are mean ± SEM of five animals. * Values are significantly different from the controls within the same age group $P < 0.05$; ** values are significantly different from young controls $P < 0.05$.

Table V
Effect of MAK on the activity of glutathione reductase

Tissue	*Young animals (10 months)*		*Old animals (32 months)*	
	Control	*Treated*	*Control*	*Treated*
Cerebral cortex	0.22 ± 0.02	0.28 ± 0.01*	0.18 ± 0.01**	0.21 ± 0.01*
Hypothalamus	0.28 ± 0.02	0.35 ± 0.03*	0.19 ± 0.02**	0.29 ± 0.03*
Rest of the cerebrum	0.26 ± 0.01	0.35 ± 0.02*	0.25 ± 0.02	0.35 ± 0.01*
Brain-stem	0.24 ± 0.01	0.32 ± 0.04*	0.23 ± 0.02	0.30 ± 0.03*
Cerebellum	0.27 ± 0.01	0.34 ± 0.02*	0.26 ± 0.02	0.33 ± 0.02*
Spinal cord	0.32 ± 0.01	0.39 ± 0.03*	0.31 ± 0.02	0.37 ± 0.02*

Notes. The activity of enzyme is expressed as micromoles of GSH formed per minute per milligram of protein. Data are mean ± SEM of five animals. * Values are significantly different from the controls within the same age group $P < 0.05$; ** values are significantly different from young controls $P < 0.05$.

Table VI
Effect of MAK on the level of endogenous TARS production

Tissue	*Young animals (10 months)*		*Old animals (32 months)*	
	Control	*Treated*	*Control*	*Treated*
Cerebral cortex	41.86 ± 1.27	32.10 ± 1.18*	82.12 ± 1.31**	42.77 ± 1.07*
Hypothalamus	32.37 ± 1.00	26.40 ± 0.79*	87.93 ± 1.37**	37.78 ± 1.17*
Rest of the cerebrum	76.89 ± 1.39	57.08 ± 1.11*	122.55 ± 1.43**	70.95 ± 1.57*
Brain-stem	43.81 ± 1.07	19.02 ± 0.78*	82.12 ± 1.59**	24.47 ± 1.71*
Cerebellum	27.68 ± 1.76	18.43 ± 0.99*	50.57 ± 1.01	29.41 ± 0.78*
Spinal cord	41.82 ± 1.08	26.70 ± 1.00*	81.40 ± 1.17**	42.17 ± 0.97*

Notes. The values are nanomoles of TARS per milligram of protein. Data are mean ± SEM of five animals. * Values are significantly different from the controls within the same age group $P < 0.05$; ** values are significantly different from young controls $P < 0.05$.

Study 13 **Research Highlights**
As demonstrated in guinea pigs, the treatment of MAK 500 mg/kg body wt for two months could augment the activities of antioxidant enzymes. Therefore, MAK could be used in compensating the decline in the activities of antioxidant enzymes in the CNS, thereby reducing the risks of lipid peroxidation.

14. Title

Effect of Maharishi Amrit Kalash, an Ayurvedic Herbal Mixture, on Lipid Peroxidation and Neuronal Lipofuscin Accumulation in Ageing Guinea Pig Brain

Publication

Indian Journal of Experimental Biology, Vol. 39, No. 4, pp. 355-359, 2001.

Authors

B.P. Vohra, S.P. Sharma, V.K. Kansal, and S.K. Gupta.

Conducted at

Laboratory of Nutritional Histopathology, Kurukshetra University, India

Summary

The effects of Ayurvedic herbal mixture Maharishi Amrit Kalash (MAK) were studied on brain lipid peroxidation, oxygen consumption, and lipofuscin accumulation in 10-month-old and 32-month-old guinea pigs. Brain regions studied were cerebral cortex, hypothalamus, cerebellum and spinal cord. Parameters assessed were lipid peroxidation, oxygen consumption, and lipofuscin accumulation. The endogenous lipid peroxide was found to be increased significantly ($P < 0.05$) in the 32-month-old animals. Neuronal lipofuscin accumulation in the neurons of cerebral motor cortex, cerebellum and cervical spinal cord was increased ($P < 0.05$) in the older animals. Oxygen consumption was found to be decreased significantly ($P < 0.05$) in the 32-month-old guinea pigs. Treatment with MAK at a dose of 500 mg/kg body weight daily for two months reduced the lipid peroxidation and lipofuscin pigment accumulation significantly in brain regions, and it also helped in restoring the normal oxygen consumption in the older animals. This indicates antioxidant properties of MAK.

Study 14 **Research Highlights**

Treating guinea pigs with MAK at a dose of 500 mg/kg body weight daily for two months reduced lipid peroxidation in brain regions and helped restore normal oxygen consumption in older animals. This indicates antioxidant properties of MAK.

15. Title

The Antioxidant Activity of Maharishi Amrit Kalash (MAK-4 and MAK-5), Estrogen and Vitamin C

Presented at

Scientific Conference on Atherosclerosis, Thrombosis, and Proliferation, American Heart Association, Orlando, FL, February 23-26, 1994.

Authors

Hari M. Sharma, Atef N. Hanna, Lynda C. Titterington, Gary P. Lubow, and Ralph E. Stephens.

Conducted at

The Ohio State University, Columbus, OH

Summary

MAK-4 and MAK-5 inhibit Cu^{+2}-catalyzed LDL oxidation and liver microsomal lipid peroxidation. In this study, we examined the ability of antioxidants to inhibit endothelial cell (EC)- and Soybean lipoxygenase (SLP)-induced LDL oxidation, and total antioxidant capacity to absorb peroxyl free radicals. Both aqueous and alcoholic extracts of MAK-4 and MAK-5 inhibited the EC-induced LDL oxidation in a concentration-dependent manner. The concentrations (ug/2mL) that produce 50% inhibition (IC_{50}) for aqueous extracts of MAK-4 and MAK-5 were 100.4 ± 6.2, 180.6 ± 17.9, and alcoholic extracts of MAK-4 and MAK-5, 57.5 ± 15.2, 7.10 ± 2.26, respectively, for TBARS. MAK-4 and MAK-5 caused prolongation of the lag phase and delay of the propagation phase of EC-LDL oxidation. Both aqueous and alcoholic extracts of MAK-4 inhibited the SLP-induced LDL oxidation in a concentration-dependent manner [IC_{50} were 840.6 ± 196.6 and 246.4 ± 32.5, respectively]. The aqueous extract of MAK-5 inhibited SLP-induced LDL oxidation in a concentration-dependent manner [IC_{50} was 503.0 ± 139.4] and Vit. C inhibited up to 35% at a concentration of 200 uM, whereas estradiol and estrone were ineffective up to 20 uM. Vit. C, MAK-4 and MAK-5 showed a concentration-dependent potency in absorbing peroxyl radicals. These results suggest that MAK-4 and MAK-5 possess antioxidant activity and might be beneficial in atherosclerosis.

Study 15 **Research Highlights**
Both aqueous and alcoholic extracts of MAK-4 and MAK-5 inhibited endothelial cell-induced LDL oxidation in a concentration-dependent manner. Thus, it is suggested that MAK-4 and MAK-5 possess antioxidant activity and might be beneficial in atherosclerosis.

16. Title

Anti-Aging Effect of a Natural Product, Maharishi Amrit Kalash (MAK)

Presented at

Joint Meeting of the International Union of Biochemists – Symposium No. 200, Satellite Meeting of the Oxygen Society, and the International Society for Free Radical Research, Berkeley, CA, January 26-27, 1990.

Authors

J.Z. Fields,* R.H. Schneider,** L. Wichlinski,* and J. Hagen.*

Conducted at

* Department of Pharmacology, Hines V.A. – Loyola University Medical Center, Maywood, IL
**Department of Physiology, Maharishi International University, Fairfield, IA

Summary

Aging is a concept that is not clearly defined. Is it the genetically coded final stage in development or the random accumulation of errors? Operationally, aging is seen as a process that increases susceptibility to disease and dysfunction. Interventions to retard or reverse this process would decrease disease, improve human function, and thereby increase quality of life and at least mean survival time.

Ayurvedic medicine, the traditional medicine of India, holds that Maharishi Amrit Kalash (MAK) has substantial anti-aging properties. Accordingly, we studied the effects of this novel herbal preparation, MAK, on aging and related parameters. MAK is a combination of 26 plants (Maharishi Ayurveda Products International, Stoneham, Massachusetts).

Fifty-eight C57BL/6 mice (males) started on dietary MAK supplements at 25 mo, and kept on them for up to 8 weeks, showed significantly ($p<0.05$) more activity (locomotion, +85%), more coordination (roto-rod, +23%) and lower heart weight (-30%).

For mice (n=58) started at 18 mo, 80% of MAK mice were alive at 23 mo vs. 48% for controls ($p<0.05$). In these survivors, body weights for controls (41.5 g) and for MAK mice (38.3 g) were not significantly different.

MAK also increased acute survival 7 days after injection of a cytotoxic drug mitomycin-c at 3.25 mg/kg: 100%

of MAK (Fisher female) rats (9 of 9) were alive compared to 33% (2 out of 6) for controls ($p<0.05$).

The finding of H. Sharma (Physiol. Biochem. Behav., in press) that MAK prevents cancer also suggests an anti-aging effect. The anti-aging mechanism(s) may include scavenging of reactive oxygen metabolites (ROM) by low molecular weight anti-oxidants. Using aqueous extracts, we found that MAK was as competent as superoxide dismutase (100% inhibition) and as potent, mg for mg, at scavenging one oxygen free radical, superoxide anions, produced by human neutrophils (PMN) (reduction of ferricytochrome-c assay). In vitro, at similar MAK concentrations, hypochlorous acid (HOCl) was also scavenged (iodometric assay). HOCl is another PMN-generated ROM and may be even more directly involved in tissue injury.

The maximum anti-aging effects of MAK, the full effects in man, and the active ingredients of MAK and their mechanisms remain to be determined.

Study 16 **Research Highlights**
MAK supplementation to mice at 18 mo and continuing to 23 mo showed increased survival rates as compared with controls. Mice started on dietary MAK supplements at 25 mo and continuing for 8 weeks showed significantly more activity, more coordination and lower heart weight. MAK also significantly increased acute survival of rats 7 days after injection of a cytotoxic drug.

17. Title
Superoxide Scavenging of Two Natural Products, Maharishi-4 [MAK-4] and Maharishi-5 [MAK-5]

Publication
Federation of American Societies for Experimental Biology Journal, Vol. 5, No. 5, p. A1284, 1991 (Abstract).

Authors
Philip F. Tomlinson, Jr. and Robert Keith Wallace (SPON: J. Fagan).

Conducted at
Department of Physiological and Biological Sciences, Maharishi International University, Fairfield, IA 52556

Summary
Maharishi Ayurveda, a recent restoration of the traditional health care system of India, upholds an herbal fruit concentrate (M-4) and an herbal tablet (M-5) as rasayanas—food supplements that promote physiological balance, health, and immunity. The superoxide scavenging properties of M-4, M-5, and ascorbic acid were investigated with superoxide radicals generated during the catalytic activity of xanthine oxidase. M-4 and M-5 (10 mg/ml prior to centrifugation) inhibited the reduction of nitroblue tetrazolium (NBT) 98% and 96%, respectively. 50% inhibition of NBT reduction was obtained with 0.04 mg/ml M-4 and 0.15 mg/ml M-5. Ascorbic acid inhibition of superoxide radical reduction of NBT reached 88% at 1 mM, but declined to 42% at a concentration of 10 mM. The rate of uric acid production monitored at 290 nm demonstrated negligible inhibition of xanthine oxidase by M-4, M-5, or ascorbic acid. The results contribute to an understanding of previously reported antineoplastic, antioxidant, and anti-aging properties of M-4 and M-5, and warrant consideration in the light of present preventive, nutritional, and chemotherapeutic approaches to health, antioxidant defense, and carcinogenesis.

Study 17 **Research Highlights**
M-4 and M-5 (10 mg/ml prior to centrifugation) inhibited the reduction of nitroblue tetrazolium 98% and 96%, respectively. The results contribute to an understanding of previously reported antineoplastic, antioxidant and anti-aging properties of M-4 and M-5.

18. Title

Oxygen Free Radical (OFR) Scavenging Effects of an Anti-Carcinogenic Natural Product, Maharishi Amrit Kalash

Publication

The Pharmacologist, Vol. 32, No. 3, p. 155, 1990 (Abstract).

Authors

Jeremy Z. Fields, Paresh A. Rawal, John F. Hagen, Todd Ing, R. Keith Wallace, Philip F. Tomlinson, and Robert H. Schneider.

Conducted at

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Dept. of Physiology, Maharishi Int'l. Univ., Fairfield, IA 52556

Summary

Recently H. Sharma et al (Pharm Bioch Behav, 35:767-773, 1990) showed that MAK, an herbal mixture derived from 15 different plants, prevents and even reverses chemically induced breast tumors in rats. Although the chemical constituents are not yet known, we hypothesized that MAK might contain one or more scavengers of OFR. Aqueous extracts of MAK (5g + 10 ml H_20), or superoxide dismutase (SOD), or vehicle were added at various dilutions to suspensions of [1] human neutrophils (PMN; 1 x 10^6 cells) prior to stimulation (by phorbol myristate acetate) or [2] xanthine/xanthine oxidase. Superoxide (SO) was monitored via reduction of ferricytochrome C followed at 550 nm. Like SOD, MAK was able to completely scavenge SO and MAK did not compromise the viability (trypan blue exclusion) or respiration (O_2 utilization) of PMNs. Thus, the anti-oxidant properties of MAK may contribute to its anti-carcinogenic properties.

Study 18 **Research Highlights**

Aqueous extracts of MAK added at various dilutions to suspensions of human neutrophils (PMNs) were able to completely scavenge superoxide and did not compromise the viability or respiration of PMNs. Thus, the anti-oxidant properties of MAK may contribute to its anti-carcinogenic properties.

19. Title

Anti-Aging and Oxygen Free Radical (OFR) Scavenging Effects of an Anti-Carcinogenic Natural Product, Maharishi Amrit Kalash [MAK-4 and MAK-5]

Publication

Federation of American Societies for Experimental Biology Journal, Vol. 5, No. 6, p. A1735, 1991 (Abstract).

Authors

J.Z. Fields, E. Eftekhari, J.F. Hagen, L.J. Wichlinski, and R.H. Schneider (SPON: A.H. Friedman).

Conducted at

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Dept. of Physiology, Maharishi International University, Fairfield, IA

Summary

MAK is an herbal preparation available as a food supplement. It is being taken for its anticipated health-promoting and anti-aging benefits. MAK refers to the combination of two natural products: M4 a paste, and M5 a tablet. Combined MAK is comprised of plants or plant parts from 24 different herbs. Sharma et al (Pharmacol Biochem Behav, 35:767-773, 1990) showed that MAK prevents and even reverses chemically induced breast tumors in rats. We showed (JZ Fields et al, The Pharmacologist, 32:155, 1990) that aqueous extracts of MAK scavenged both OFR (superoxide) and non-radical oxidants (hypochlorous acid) in suspensions of human neutrophils without compromising the viability of the cells. In mice (C57BL/6 male, n=29/group) fed 6% MAK in the diet starting at 18 months of age, 80% of MAK mice were alive at 23 mo vs. 48% for controls ($p < 0.05$). Body weights for control (41.5 g) and MAK mice (38.3 g) were not significantly different. In fruitflies (male, wild type, Drosophila melanogaster, n=100/group) fed 12% MAK from hatching to expiration, mean life span was significantly increased (+70%). The anti-oxidant properties and anti-carcinogenic properties of MAK may contribute to its anti-aging properties.

Study 19 **Research Highlights**
Studies have been conducted in animals and in vitro demonstrating the antioxidant properties and anti-carcinogenic properties of MAK, which may contribute to its anti-aging properties.

20. Title

Anti-Oxidant and Antiplatelet Properties of Maharishi Amrit Kalash [MAK-4] in Hypercholesterolemic Rabbits

Publication

Ninth International Symposium on Atherosclerosis, Rosemont, IL, October 6-11, 1991, p. 188 (Abstract).

Authors

Rao V. Panganamala, Ph.D. and Hari M. Sharma, M.D., FRCP(C).

Conducted at

The Ohio State University, College of Medicine, Columbus, OH, USA

Summary

Platelet aggregation and oxidized lipids are considered important mediators of vascular injury leading to atherosclerosis. M-4, an herbal food supplement (MAPI Inc., Lancaster, MA) has been shown to be effective in preventing generation of reactive oxygen species in-vitro (IJCP 1:23-27, 1991). The experiments were carried out to evaluate the effectiveness of M-4 in preventing platelet aggregation and oxidation of lipids in hypercholesterolemic rabbits. Two groups of six rabbits (pair matched) were given a 1% cholesterol diet. The experimental group in addition was given 0.4% M-4 in the diet. At the end of the experiment (7 weeks) total cholesterol, plasma and hepatic TBARS and platelet aggregation induced by ADP & collagen were compared between the two groups. The results are:

	Control	Experimental
Total cholesterol (mg/dl)	1511	1003
Plasma TBARS (nmoles/ml)	5.38 ± 0.5	1.9 ± 0.3
Hepatic TBARS (nmoles/g tissue)	148 ± 16	83 ± 11

Platelet Aggregation	% Transmittance			
	Collagen (ug/ml)		ADP (x 10^{-3})	
	4.4	2.2	4.4	2.2
Control (n = 5)	48.6	30.0	34.0	21.0
Experimental (n = 4)	26.0	3.0	10.0	3.75

Results show that M-4 supplementation reduces plasma and hepatic lipid peroxidation and platelet aggregation induced by collagen and ADP in hypercholesterolemic rabbits.

Study 20 **Research Highlights**

M-4 supplementation reduced plasma and hepatic lipid peroxidation and platelet aggregation induced by collagen and ADP in hypercholesterolemic rabbits.

21. Title

Lipid Peroxide in Ischemic Heart Disease (IHD): Inhibition by Maharishi Amrit Kalash (MAK-4 and MAK-5) Herbal Mixtures

Publication

Federation of the American Societies for Experimental Biology Journal, Vol. 14, No. 4, p. A121, 2000 (Abstract).

Authors

J. Dogra and A. Bhargava (SPON: H. Sharma).

Conducted at

Central Government Health Scheme and Okay Research Centre, Jaipur, India 302017

Summary

As oxidation of low-density lipoprotein plays a significant role in atherogenesis, an improvement in the antioxidant status should lead to a protective effect. We initiated this trial to study the in vivo effects of MAK-4 and MAK-5 (herbal mixtures containing polyphenols, bioflavonoids, tocopherol, ascorbic acid, and carotenoids) on lipid peroxide in addition to its clinical efficacy. Eighty patients with proven IHD were enrolled in our study. Lipid peroxide studies were done initially and at one year in MAK-supplemented and control groups. The control group consisted of 40 IHD patients minus MAK. Drugs like antioxidant vitamin E and lipid-lowering agents were withdrawn in both groups. Clinical parameters of drug response were assessed. MAK-4 paste was prescribed in a dose of 10 g daily in 2 divided doses followed by MAK-5 tablet, for 1 year as 'add-on' regimen. Thirty-four patients reported a significant decrease in the mean anginal frequency per month from 5.50 (+3.20) to 2.15 (+2.00) and improvement in the treadmill test was reported in 8 cases at 1 year. Echocardiography studies reported improvement in ejection fraction in 7 cases. Plasma lipid peroxide concentration of patients with IHD was 7.24 nmoles MDA/ml (mean), which was reduced to 4.97 nmoles MDA/ml (mean) after 1 year of MAK 'add-on' trial. However, no significant reduction was noted in the control group. We conclude that MAK significantly lowers lipid peroxide, which has been implicated in atherogenesis and significantly lowers the incidence of myocardial ischemia.

Study 21 **Research Highlights**

Plasma lipid peroxide concentration of patients with Ischemic Heart Disease was reduced from 7.24 nmoles MDA/ml (mean) to 4.97 nmoles (mean) after 1 year of MAK supplementation, while no significant reduction was noted in the control group. Thus, MAK significantly lowers lipid peroxide, which has been implicated in atherogenesis and significantly lowers the incidence of myocardial ischemia.

Cardiovascular Research

1. Title

Effect of Herbal Mixtures MAK-4 and MAK-5 on Susceptibility of Human LDL to Oxidation

Publication

Complementary Medicine International, Vol. 3, No. 3, pp. 28-36, May/June 1996.

Authors

Atef N. Hanna, PhD,* Vidya Sundaram, MD,** James M. Falko, MD,** Ralph E. Stephens, PhD,* and Hari M. Sharma, MD, FRCPC.*

Conducted at

*Department of Pathology and **Department of Internal Medicine, College of Medicine, The Ohio State University, Columbus, OH 43210

Summary

Oxidation of low-density lipoprotein (LDL) plays a central role in the pathogenesis of atherosclerosis. This study investigated the in vivo antioxidant activity of MAK-4 and MAK-5 in a clinical setting, and investigated the in vitro antioxidant properties of MAK-4. Both the aqueous and alcoholic extracts of MAK-4 inhibited endothelial cell (EC)- and soybean lipoxygenase (SLP)-induced LDL oxidation in a concentration-dependent manner. The agent concentrations (microgram/mL) which inhibited 50% (IC_{50}) of EC- and SLP-induced LDL oxidation, respectively, were 150.0 +/- 10.0 and 488.3 +/- 41.9 for the aqueous extract, and 69.3 +/- 8.1 and 128.3 +/- 18.9 for the alcoholic extract. In vitro pretreatment of LDL with MAK-4 increased the resistance of LDL to Cu^{+2}-catalyzed LDL oxidation. Both the aqueous and alcoholic extracts inhibited

Figure 1a.

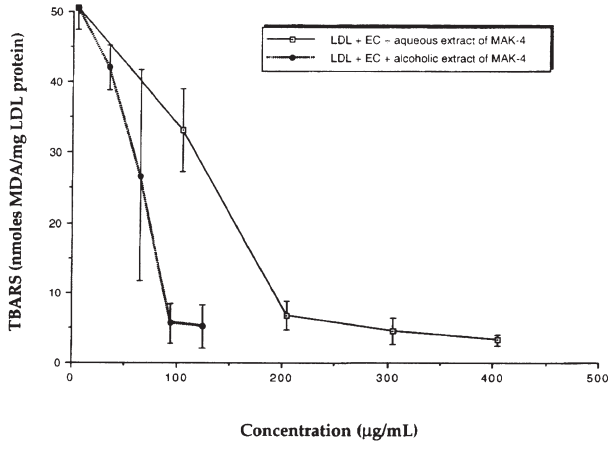
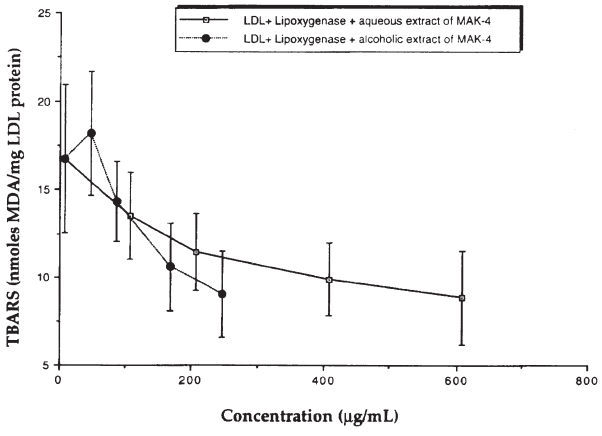


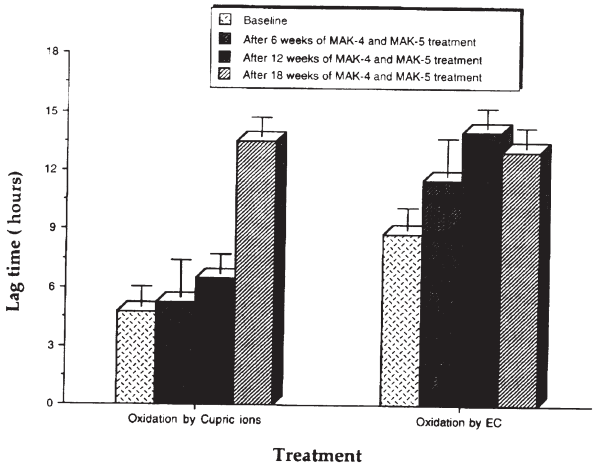
Figure 1b.



The effect of the aqueous and alcoholic extracts of MAK-4 on endothelial cell (EC)- induced LDL oxidation (Figure 1a.) and soybean lipoxygenase (SLP)-induced LDL oxidation (Figure 1b.). LDL (200 µg LDL protein) was incubated with or without EC or 20 mg/mL of SLP, in the presence or absence of various concentrations of the aqueous or alcoholic extracts of MAK-4, in a humidified environment of 95 percent air and 5 percent CO_2, at 37°C. for 24 hours. The degree of LDL oxidation was assessed by measuring thiobarbituric acid- reactive substances (TBARS). All values are expressed as mean ± SD, n=three subjects.

free radical generation in a concentration-dependent manner. The IC_{50} was 16.35 +/- 4.27 for the aqueous extract, and 3.64 +/- 1.24 for the alcoholic extract; addition of both extracts showed a synergistic interaction. In hyperlipidemic patients, MAK-4 and MAK-5 increased resistance of LDL to oxidation by Cu^{+2} and EC. These results suggest that MAK-4 and MAK-5 protect LDL from oxidation and may be useful in the prevention and treatment of atherosclerosis.

Figure 4.



Effect of treatment of hyperlipidemic patients with MAK-4 and MAK-5 on the susceptibility to Cu^{+2}- or endothelial cell (EC)-induced LDL oxidation, as assessed by measuring the lag time of the oxidative process. LDL was isolated from hyperlipidemic patients before, and six, 12, and 18 weeks after treatment with MAK-4 and MAK-5. Isolated LDL was incubated with two mmol/L Cu^{+2} at 37°C., in an atmosphere of humidified 95 percent air and 5 percent CO_2. Samples were taken at zero, one, two, three, four, six, eight, 10, 12, 14, and 24 hours, and stored with 0.1 mmol/L EDTA at -80°C. The same method was used to test resistance to EC-induced LDL oxidation, except samples were taken at zero, three, six, eight, 10, 12, 14, and 24 hours. The degree of LDL oxidation was assessed by measuring TBARS. All values are expressed as mean ± SD, n=four subjects.

Study 1 **Research Highlights**
MAK-4 and MAK-5 increased resistance of LDL to oxidation by Cu^{+2} and EC in hyperlipidemic patients. These results suggest that MAK-4 and MAK-5 protect LDL from oxidation and may be useful in the prevention and treatment of atherosclerosis.

2. Title

Inhibition of Low-Density Lipoprotein Oxidation by Oral Herbal Mixtures Maharishi Amrit Kalash-4 (MAK-4) and Maharishi Amrit Kalash-5 (MAK-5) in Hyperlipidemic Patients

Publication

The American Journal of the Medical Sciences, Vol. 314, No. 5, pp. 303-310, 1997.

Authors

Vidya Sundaram, M.D.,* Atef N. Hanna, Ph.D.,** Gary P. Lubow, M.D.,** Lata Koneru, M.D.,† James M. Falko, M.D.,* and Hari M. Sharma, M.D.**

Conducted at

*Department of Internal Medicine and **Department of Pathology, College of Medicine, The Ohio State University, Columbus, OH

†Department of Internal Medicine, Riverside Methodist Hospital, Columbus, OH.

Summary

Low-density lipoprotein (LDL) oxidation is central to the pathogenesis of atherosclerosis. This study evaluated the antioxidant activity of MAK-4 and MAK-5 in vivo. Ten hyperlipidemic patients prescribed stable hypolipidemic therapy were treated with MAK-4 and MAK-5 for 18 weeks. Plasma lipoprotein, plasma lipid peroxide, and LDL oxidation studies were performed every 6 weeks. Apolipoprotein A, apolipoprotein B, and lipoprotein (a) levels were measured at baseline and 18 weeks. After 12 weeks of treatment with MAK-4 and MAK-5, a time-dependent increase in the lag phase and delay in the propagation phase of oxidation of LDL by Cu^{+2} and endothelial cells was seen. Lag phases at baseline and after 6, 12, and 18 weeks of MAK-4 and MAK-5 ingestion were 6.66 hours ± 0.19 (mean ± standard error of mean), 6.77 hours ± 0.31, 7.22 hours ± 0.24, and 18.00 hours ± 0.73, respectively, for Cu^{+2}-catalyzed LDL oxidation. Lag phases were 14.89 hours ± 0.77, 13.33 hours ± 0.50, 20.22 hours ± 0.76, and 20.00 hours ± 0.79, respectively, for endothelial cell-induced LDL oxidation. The levels of plasma lipid peroxide did not change significantly. No significant changes were seen in the plasma lipoproteins and the levels of apolipoprotein A, apolipoprotein B, and lipoprotein (a). The results show that MAK-4 and MAK-5 inhibit LDL oxidation in patients with hyperlipidemia. Therefore, MAK-4 and MAK-5 may be useful in the prevention and treatment of atheroslerosis.

See Antioxidant Research for more information on this study.

Study 2 **Research Highlights**

Ten hyperlipidemic patients were treated with MAK-4 and MAK-5 for 18 weeks. After 12 weeks of treatment with MAK-4 and MAK-5, a time-dependent increase in the lag phase and delay in the propagation phase of oxidation of LDL by Cu^{+2} and endothelial cells was seen. Therefore, MAK-4 and MAK-5 may be useful in the prevention and treatment of atherosclerosis.

3. Title

The Antioxidant and Antiatherogenic Effects of MAK-4 in WHHL Rabbits

Publication

Journal of Alternative and Complementary Medicine, Vol. 2, No. 4, pp. 463-478, 1996.

Authors

Jae Y. Lee, PhD, Atef N. Hanna, PhD, John A. Lott, PhD, and Hari M. Sharma, MD, FRCPC.

Conducted at

Department of Pathology, College of Medicine, The Ohio State University, Columbus, OH 43210

Summary

This study tested the effect of MAK-4 on the development of atheroma in WHHL rabbits. Eleven rabbits were divided into two groups: controls (n = 5) and a group fed 6% (w/w) MAK-4 (n = 6). Blood was drawn for biochemical analysis every two months and at necropsy, six months after the special diet was started. The aortas were preserved in formalin. The percentage area of aortic arch covered with visible plaque in the MAK-4 group (22.5 ± 4.2%, mean ± SE) was significantly reduced (p <0.01) compared to the control group (47.6 ± 6.8%, mean ± SE). The MAK-4 group showed a significant decrease (p <0.05) in lipid peroxide, and a significant increase (p <0.05) in glutathione peroxidase and resistance of LDL to endothelial cell-induced and cupric ion-catalyzed oxidation (4.5 h and 5 h lag phase, respectively, for the MAK-4 group; 0 h lag phase for both for the controls). These findings suggest MAK-4 reduces atheroma formation through its antioxidant activity.

See Antioxidant Research for more information on this study.

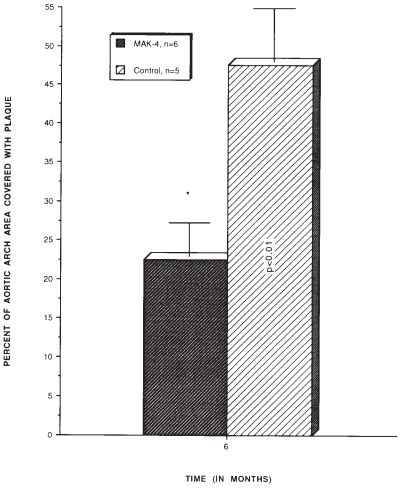


Fig. 8. Effects of MAK-4 on plaque formation on aortic arch in WHHL rabbits (22.5±4.2% and 47.6±6.8% for MAK-4 group and control group, respectively; values are mean ± SE). *p<0.01

Study 3 **Research Highlights**
As compared with a control group, WHHL rabbits treated with MAK-4 for 6 months showed a significant reduction in visible plaque in the aortic arch and a significant increase in resistance of LDL to induced oxidation. It is suggested that MAK-4 reduces atheroma formation through its antioxidant activity.

4. Title

Inhibition of Human Low-Density Lipoprotein Oxidation In Vitro by Maharishi Ayur-Veda Herbal Mixtures [MAK-4, MAK-5, MA-631, and Maharishi Coffee Substitute]

Publication

Pharmacology, Biochemistry and Behavior, Vol. 43, pp. 1175-1182, 1992.

Authors

Hari M. Sharma, Atef N. Hanna, Ellen M. Kauffman, and Howard A.I. Newman.

Conducted at

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Summary

In this study on the in vitro inhibition of human LDL oxidation, the rasayanas (health-promoting herbal mixtures) MAK-4, MAK-5, MA-631, and Maharishi Coffee Substitute, were compared to the antioxidants vitamin C, vitamin E, and probucol (an antioxidant drug). All four rasayanas showed more than a 1000-fold greater inhibition of cupric ion-catalyzed LDL oxidation, as compared to vitamin C, vitamin E, and probucol (p<0.0001).

For more information on this study, see Antioxidant Research.

Study 4 **Research Highlights**
MAK-4, MAK-5, MA-631, and Maharishi Coffee Substitute showed more than a 1000-fold greater inhibition of cupric ion-catalyzed LDL oxidation, as compared to vitamin C, vitamin E, and probucol.

5. Title

Maharishi Amrit Kalash (MAK-5) Prevents Human Platelet Aggregation

Publication

Clinica and Terapia Cardiovascolare, Vol. 8, No. 3, pp. 227-230, 1989.

Authors

H.M. Sharma,* Y. Feng,** and R.V. Panganamala.**

Conducted at

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Summary

MAK-5 belongs to a group of substances which are known as "rasayanas." The purpose of rasayanas is two-fold: prevention of disease and retardation or reversal of the aging process, which results from optimization of physiological balance (homeostasis). This investigation was conducted to study the effect of MAK-5 on human platelet aggregation. Platelet aggregation can be induced by free radicals, catecholamines, and vascular linings injured by oxidized lipids. This in vitro experiment showed that MAK-5 reduces platelet aggregation in platelet-rich plasma obtained from normal, healthy subjects. This prevention of aggregation was seen with the following inducers of platelet aggregation: catecholamines, which are released during stress; collagen, which is exposed when vascular endothelium is injured; arachidonic acid, which is released from injured cell membranes; and ADP, which is released from injured red blood cells and platelets. Since platelet aggregation is considered an important aspect of the initiation and progression of atherosclerosis, the ability of MAK-5 to reduce platelet aggregation may help in the prevention of atherosclerosis.

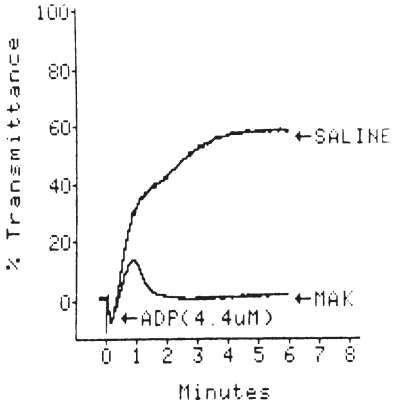

Fig. 1 - Effect of MAK on epinephrine induced platelet aggregation. This shows blockage of second phase of epinephrine induced aggregation.

		% Aggregation		
Agonist	Dose	Control	MAK	Significance
Collagen	0.28 ug/ml	56.6 ± 4.1*	0	$p < 0.001$
ADP	11 uM	49.4 ± 6.6*	22.4 ± 7.2	$p < 0.05$

* ± SEM
Number of subjects = 9

Table 3 - Inhibition of platelet aggregation by MAK in whole blood.

Study 5 **Research Highlights**

This in vitro experiment showed that MAK-5 reduces platelet aggregation in platelet-rich plasma obtained from normal, healthy subjects. Since platelet aggregation is considered an important aspect of the initiation and progression of atherosclerosis, the ability of MAK-5 to reduce platelet aggregation may help in the prevention of atherosclerosis.

6. Title

Indigenous Free Radical Scavenger MAK-4 and MAK-5 in Angina Pectoris. Is it Only a Placebo?

Publication

Journal of the Association of Physicians of India, Vol. 42, No. 6, pp. 466-467, 1994.

Authors

J. Dogra,* N. Grover,* P. Kumar,* and N. Aneja.**

Conducted at

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**SMS Medical College, Jaipur, India

Summary

Thirty patients were evaluated to study the effect of Maharishi Amrit Kalash (MAK-4 and MAK-5) on angina pectoris. The mean angina frequency per month was 8.87. Twelve lead ECG, computerized TMT and echo studies were done initially, at 6 months, and after 2 years in all cases. Ten grams of MAK-4 paste was given daily in two divided doses, each followed by a MAK-5 tablet, for six months. Vasodilator and antihypertensive drugs were continued on ethical grounds. Twenty-four patients (80%) of the total 30 reported a significant improvement after 6 months of therapy. The mean angina frequency per month improved from 8.87 to 3.03 ($p<0.001$). All patients reported a sense of well-being. Five of 11 hypertensive patients reported a fall in systolic blood pressure. The lipid profile showed a rise in high-density lipoprotein (HDL) which was statistically insignificant. Improved exercise tolerance was observed in 10 cases (33.33%) after 6 months of therapy and this effect was sustained even at 2 years. ECG and echo studies were inconclusive. No side effects or drug interactions were seen. The beneficial effects observed may be the result of the free radical-scavenging property of MAK-4 and MAK-5 on reactive oxygen species (ROS), or an inhibitory effect on lipid peroxidation, or inhibition of platelet aggregation, or all of these in synergism.

TABLE 1. Showing Changes in anginal status after MAK-4 and MAK-5 (n= 30).

Chest pain	Mean (± SD) at base line	Mean (± SD) at 6 months	Mean (± SD) at 2 years
Frequency* per month	8.87 (± 7.18)	3.03 (± 3.74)	3.57 (± 3.96)
Duration (in mins)	2.70 (± 4.50)	1.89 (± 4.30)	2.02 (± 4.21)
Severity**	3.1 (± 1.4)	2.4 (± 1.3)	2.45 (± 1.4)
Sub-lingual tablets consumed per month*	17.37 (± 12.59)	5.8 (± 5.79)	7.33 (± 6.96)

* Applying X^2 test $p < 0.001$.

** Scale of 1 to 7 (1 indicating least severe)

Study 6 **Research Highlights**

Eighty percent of patients reported improvement in angina pectoris after 6 months of MAK-4 and MAK-5 therapy, with the mean angina frequency improving from 8.87 to 3.03 ($p<0.001$). The positive effects may be the result of the free radical-scavenging property of MAK-4 and MAK-5 on reactive oxygen species, or an inhibitory effect on lipid peroxidation, or inhibition of platelet aggregation, or all of these in synergism.

7. Title

Effect of Maharishi AK-4 [MAK-4] on H_2O_2-induced Oxidative Stress in Isolated Rat Hearts

Publication

Journal of Ethnopharmacology, Vol. 56, pp. 215-222, 1997.

Authors

William J. Cullen,* Scott A. Dulchavsky,* Thomas P.A. Devasagayam,* B.V. Venkataraman,** Saradindu Dutta.†

Conducted at

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Summary

Oxidative damage to crucial biomolecules due to excess generation of reactive oxygen species has been implicated as a major cause of organ damage, and hence compounds capable of negating such damage have potential benefits. Using hydrogen peroxide (H_2O_2) as a model pro-oxidant to induce oxidative stress, we have examined the ability of the natural food supplement Maharishi Amrit Kalash (MAK-4) to decrease oxidative damage in potassium-arrested isolated rat hearts. The protocol was that hearts isolated from male Sprague-Dawley rats were retrograde-perfused with Krebs-Henseleit (K-H) solution for 30 min for equilibration. After this period, the hearts were subjected to cardioplegia with high potassium (26-30 mM), followed by reperfusion with K-H solution in the presence or absence of 200 uM H_2O_2. As expected, H_2O_2 treatment following cardioplegia induced a high degree of oxidative stress as assessed by release of lactate dehydrogenase (LDH, a marker of plasma membrane damage) and total glutathione (GSH + GSSG). H_2O_2 also impaired the ability of the heart to regain developed tension during the testing period. However, addition of MAK-4 in the perfusate containing H_2O_2 decreased oxidative stress in terms of release of LDH and glutathione. In parallel with these biochemical studies, in a few experiments the cardiac function was assessed by measuring developed contractile tension. These preliminary studies also showed that in the presence of MAK-4, the H_2O_2 -treated hearts were able to regain better-developed tension. Further in vitro studies to examine the possible mechanisms of MAK-4 action reveal that this formulation contains H_2O_2 binding activity, which resulted in the decreased availability of H_2O_2 itself. Our studies hence reveal that the ayurvedic food supplement MAK-4 may have potential benefits in reducing oxidative stress.

(See charts on next page.)

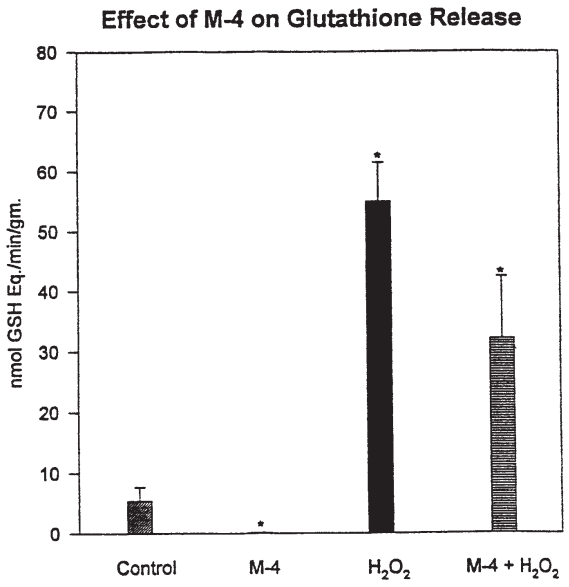

Fig. 1. Glutathione (GSH + GSSG) release into effluent samples collected at 89- to 90-min time interval from vehicle (control), MAK-4 (0.1%), 200 μM H_2O_2 and MAK-4 (0.1%) + 200 μM H_2O_2 treated isolated rat hearts. Hearts were equilibrated for 30 min, exposed to cardioplegia with high potassium (26–30 mM) for the next 45 min and reperfused with K–H for the last 30 min. Values represent mean ± SE ($n = 4$).

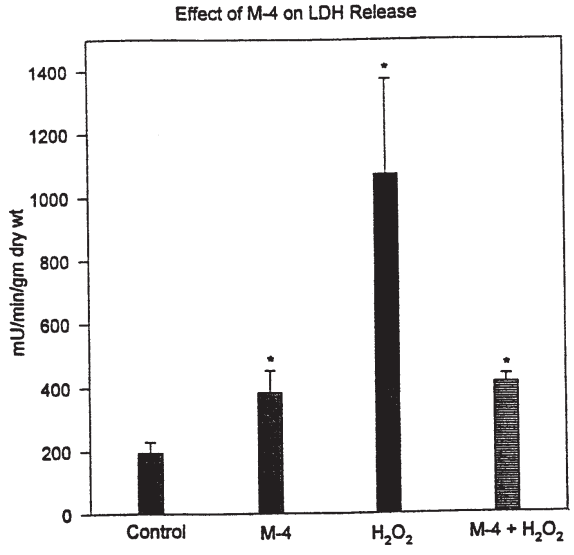

Fig. 2. Lactate dehydrogenase (LDH) release into effluent samples collected as described in Fig. 1. Values represent mean ± SE ($n = 4$).

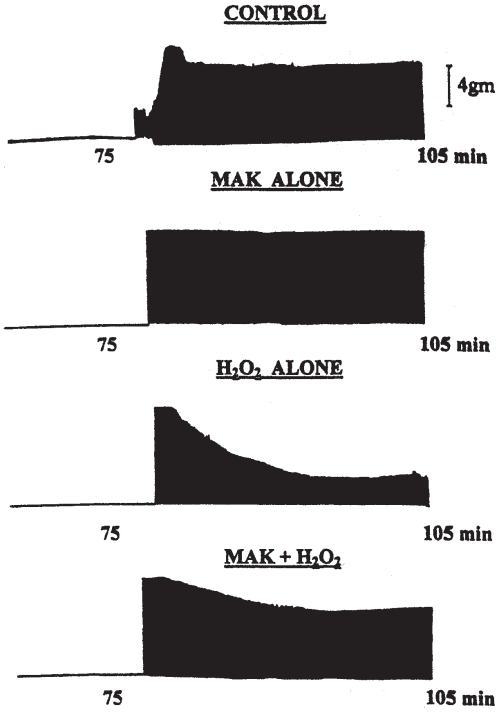

Fig. 3. Representative contractile records showing the recovery of cardioplegic, isolated rat hearts exposed to Krebs-Henseleit solution containing the following agents: (a) vehicle (control); (b) MAK-4 (0.1%); (c) 200 μM H_2O_2; (d) MAK-4 (0.1%) + 200 μM H_2O_2.

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Study 7 **Research Highlights**

Researchers demonstrated the ability of MAK-4 to successfully decrease oxidative stress induced by H_2O_2 in an in vitro model. It was subsequently found that MAK-4 contains H_2O_2 binding activity. Thus MAK-4 may have potential benefits in reducing oxidative stress.

8. Title

Anti-Oxidant and Antiplatelet Properties of Maharishi Amrit Kalash [MAK-4] in Hypercholesterolemic Rabbits

Publication

Ninth International Symposium on Atherosclerosis, Rosemont, IL, October 6-11, 1991, p. 188 (Abstract).

Authors

Rao V. Panganamala, Ph.D. and Hari M. Sharma, M.D., FRCP(C).

Conducted at

The Ohio State University, College of Medicine, Columbus, OH, USA

Summary

Platelet aggregation and oxidized lipids are considered important mediators of vascular injury leading to atherosclerosis. M-4, an herbal food supplement (MAPI Inc., Lancaster, MA) has been shown to be effective in preventing generation of reactive oxygen species in-vitro (IJCP 1:23-27, 1991). The experiments were carried out to evaluate the effectiveness of M-4 in preventing platelet aggregation and oxidation of lipids in hypercholesterolemic rabbits. Two groups of six rabbits (pair matched) were given a 1% cholesterol diet. The experimental group in addition was given 0.4% M-4 in the diet. At the end of the experiment (7 weeks), total cholesterol, plasma and hepatic TBARS, and platelet aggregation induced by ADP & collagen were compared between the two groups. The results are:

	Control	Experimental
Total cholesterol (mg/dl)	1511	1003
Plasma TBARS (nmoles/ml)	5.38 ± 0.5	1.9 ± 0.3
Hepatic TBARS (nmoles/g tissue)	148 ± 16	83 ± 11

Platelet Aggregation	% Transmittance			
	Collagen (ug/ml)		ADP (x 10^{-3})	
	4.4	2.2	4.4	2.2
Control (n = 5)	48.6	30.0	34.0	21.0
Experimental (n = 4)	26.0	3.0	10.0	3.75

Results show that M-4 supplementation reduces plasma and hepatic lipid peroxidation, as well as platelet aggregation induced by collagen and ADP, in hypercholesterolemic rabbits.

Study 8 **Research Highlights**

Hypercholesterolemic rabbits supplemented with M-4 for 7 weeks showed a reduction in plasma and hepatic lipid peroxidation, as well as platelet aggregation induced by collagen and ADP.

9. Title

Lipid Peroxide in Ischemic Heart Disease (IHD): Inhibition by Maharishi Amrit Kalash (MAK-4 and MAK-5) Herbal Mixtures

Publication

Federation of the American Societies for Experimental Biology Journal, Vol. 14, No. 4, p. A121, 2000 (Abstract).

Authors

J. Dogra and A. Bhargava (SPON: H. Sharma).

Conducted at

Central Government Health Scheme and Okay Research Centre, Jaipur, India 302017

Summary

As oxidation of low-density lipoprotein plays a significant role in atherogenesis, an improvement in the antioxidant status should lead to a protective effect. We initiated this trial to study the in vivo effects of MAK-4 and MAK-5 (herbal mixtures containing polyphenols, bioflavonoids, tocopherol, ascorbic acid, and carotenoids) on lipid peroxide in addition to its clinical efficacy. Eighty patients with proven IHD were enrolled in our study. Lipid peroxide studies were done initially and at one year in MAK-supplemented and control groups. The control group consisted of 40 IHD patients minus MAK. Drugs like antioxidant vitamin E and lipid-lowering agents were withdrawn in both groups. Clinical parameters of drug response were assessed. MAK-4 paste was prescribed in a dose of 10 g daily in 2 divided doses followed by MAK-5 tablet, for 1 year as 'add-on' regimen. Thirty-four patients reported a significant decrease in the mean anginal frequency per month from 5.50 (+3.20) to 2.15 (+2.00) and improvement in the treadmill test was reported in 8 cases at 1 year. Echocardiography studies reported improvement in ejection fraction in 7 cases. Plasma lipid peroxide concentration of patients with IHD was 7.24 nmoles MDA/ml (mean), which was reduced to 4.97 nmoles MDA/ml (mean) after 1 year of MAK 'add-on' trial. However, no significant reduction was noted in the control group. We conclude that MAK significantly lowers lipid peroxide, which has been implicated in atherogenesis and significantly lowers the incidence of myocardial ischemia.

Study 9 **Research Highlights**

Plasma lipid peroxide concentration of patients with Ischemic Heart Disease was reduced from 7.24 nmoles MDA/ml (mean) to 4.97 nmoles (mean) after 1 year of MAK supplementation, while no significant reduction was noted in the control group. Thus, MAK significantly lowers lipid peroxide, which has been implicated in atherogenesis and significantly lowers the incidence of myocardial ischemia.

10. Title

In-Vitro Inhibition of Microsomal Lipid Peroxidation by MA-631, Student and Ladies Rasayana (SR and LR) and Maharishi Coffee Substitute (MCS)

Publication

The Pharmacologist, Vol. 34, No. 3, p. 184, 1992 (Abstract).

Authors

H.M. Sharma, A. Hanna, E.M. Kauffman, and H.A.I. Newman (SPON: D. Feller).

Conducted at

College of Medicine, The Ohio State University, Columbus, OH 43210

Summary

MCS, MA-631, M-4, and M-5 have been shown to inhibit in-vitro human LDL oxidation. In the present study, the effects of MA-631, SR, LR and MCS on microsomal lipid peroxidation were examined in vitro. Rat liver microsomes were incubated with a sodium ascorbate and ADP-iron complex or with an NADPH generating system to stimulate non-enzymatic or enzymatic lipid peroxidation respectively. Aqueous or alcoholic extracts of MA-631, SR, LR and MCS, when added to these incubation systems, inhibited hepatic microsomal lipid peroxidation in a dose dependent manner. The alcoholic extracts were the most effective antiperoxidants in both systems. Alcoholic extract of MCS inhibited ascorbate or NADPH-induced lipid peroxidation by 56% and 63% with 12 ugm and 22.5 ugm, respectively. These findings suggest that these Maharishi Ayurveda food supplements may be useful in the treatment of free radical induced injury due to their antiperoxidant properties.

Study 10 **Research Highlights**

In vitro aqueous and alcoholic extracts of MA-631, Student Rasayana, Ladies Rasayana, and Maharishi Coffee Substitute demonstrated potent antiperoxidant properties in a dose-dependent manner. Thus, these supplements may be useful in the treatment of free radical-induced injury due to their antiperoxidant properties.

Diabetes Research

1. **Title**
   Hypoglycemic, Hypolipidemic and General Beneficial Effects of an Herbal Mixture MA-471

Publication
Alternative Therapies in Clinical Practice, Vol. 3, No. 5, pp. 26-31, September/October 1996.

Authors
Amulya R. Sircar, MD,* Ramesh C. Ahuja, MD,* Shankar M. Natu, PhD,* Birendra Roy, MBBS,* and Hari M. Sharma, MD, FRCPC.**

Conducted at
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**The Ohio State University, College of Medicine, Columbus, OH

Summary

An herbal mixture used for thousands of years in India for treatment of diabetes was evaluated for its efficacy and safety in patients with non-insulin-dependent diabetes mellitus (NIDDM). This herbal mixture, MA-471 (Glucomap™), was developed by Maharishi Ayur-Veda Products (Noida, India) and showed very good results in preliminary trials. In the present pilot study, a clinical trial was conducted in which patients were divided into three groups: Group A (15 cases) were patients who had never taken an anti-diabetic drug and were uncontrolled by diet and exercise; Group B (30 cases) were patients controlled by an oral hypoglycemic agent (OHA); and Group C (15 cases) were patients uncontrolled by the maximum dose of an OHA. All patients were started on MA-471 tablets after initial evaluation and blood collection, and were called for follow-up every two weeks for blood collection and observation of the improvement or deterioration of various symptoms. The mean fasting and postprandial blood glucose, and hemoglobin A_1C showed a significant decrease from the initial values in all three groups of patients. "Good" and "acceptable" control was achieved in 68.3% of the patients.

MA-471 seemed to be more effective in patients who had diabetes of less than five years duration.

MA-471 also resulted in a significant fall in serum total cholesterol and triglycerides, and resulted in marked improvement in polyuria, fatigue, and constipation. This pilot study shows the herbal mixture MA-471 has significant hypoglycemic and hypolipidemic properties, and also improves the quality of life of NIDDM patients.

(See charts on next two pages.

Table 1. Fasting and postprandial blood glucose and hemoglobin A_1C before and after MA-471.*

Group			Initial	After MA-471 3 months	6 months	9 months
A		n	15	15	15	13
	Fast. glucose		9.28(± 1.22)	7.28 (± 1.11)	6.77 (± 0.95)	6.82 (± 0.82)
		p value		< 0.001	< 0.001	< 0.001
	PP glucose		16.10 (± 1.57)	12.82 (± 1.28)	12.35 (± 1.11)	12.16 (± 1.06)
		p value		< 0.001	< 0.001	< 0.001
	HBA_1C		10.3 (± 2.8)	8.5 (± 1.49)	7.1 (± 1.5)	7.3 (± 1.47)
		p value		<0.05	< 0.01	< 0.05
B		n	30	30	30	25
	Fast. Glucose		6.43 (± 1.14)	5.90 (± 1.35)	5.54 (± 1.22)	5.70 (± 1.28)
		p value				
	PP glucose		9.55 (± 1.07)	9.10 (± 1.02)	9.37 (± 1.24)	9.45 (± 1.36)
		p value				
	HBA_1C		7.0 (± 1.97)	7.1 (± 2.1)	7.8 (± 1.87)	7.6 (± 2.8)
		p value				
C		n	15	15	15	12
	Fast. glucose		8.34 (± 1.21)	6.14 (± 1.07)	6.01 (± 0.95)	5.66 (± 0.79)
		p value		< 0.001	< 0.001	< 0.001
	PP glucose		13.73 (± 1.24)	10.33 (± 1.0)	9.51 (± 1.01)	9.42 (± 0.75)
		p value		< 0.001	< 0.001	< 0.001
	HBA_1C		10.1 (± 2.5)	8.0 (± 1.7)	7.3 (± 1.8)	6.4 (± 1.5)
		p value			< 0.01	< 0.05
TOTAL		n	60	60	60	50
	Fast. glucose		7.13 (± 1.27)	5.93 (± 1.01)	5.75 (± 0.98)	5.76 (± 1.02)
		p value		< 0.001	< 0.001	< 0.001
	PP glucose		13.07 (± 1.39)	9.91 (± 1.18)	9.54 (± 0.90)	9.67 (± 0.87)
		p value		< 0.001	< 0.001	< 0.001
	HBA_1C		9.13 (± 2.9)	7.53 (± 1.8)	6.73 (± 1.7)	6.93 (± 1.8)
		p value		< 0.01	< 0.001	< 0.01

* Values are mean ± SD. Glucose units are mmol/dL and hemoglobin A_1C unit is percent. P values were derived by comparison with initial value. Fast. glucose = fasting glucose; PP glucose = Postprandial glucose; HBA_1C = hemoglobin A_1C.

Table 5. Comparative effect of MA-471 and oral hypoglycemic agents (OHA) on some common symptoms of diabetes

	Initial	After MA-471			Initial	After OHA		
Presenting complaint	**n**	**Same**	**Improved**	**Worse**	**n**	**Same**	**Improved**	**Worse**
Polyuria	25	5	18	2	27	10	13	4
Polydipsia	13	3	6	4	11	5	4	2
Mouth dryness	12	8	4	-	15	10	3	2
Weakness	41	19	21	1	39	24	10	5
Fatigue	39	15	23	1	42	23	12	7
Joint pain	33	21	10	2	34	24	10	-
Muscle pain	28	16	11	1	26	18	6	2
Giddiness	33	16	15	2	30	20	10	-
Nausea	3	2	1	-	2	2	-	-
Anorexia	26	13	10	3	22	14	8	-
Constipation	15	7	8	-	16	8	6	2
Abdominal pain	6	5	1	-	4	4	-	-
Palpitation	18	11	7	-	20	9	9	2
Paresthesia	23	19	3	1	26	20	3	3
Numbness	30	23	5	2	29	24	4	1
Pruritis	2	1	1	-	1	1	-	-
Anxiety	13	9	4	-	13	9	2	2
Insomnia	19	13	6	-	17	12	5	-
Headache	2	2	-	-	1	1	-	-
Skin rash	4	1	3	-	2	1	-	1
Impotence	15	10	5	-	13	13	-	-

Study 1 **Research Highlights**
Supplementation of Non-Insulin Dependent Diabetes Mellitus (NIDDM) patients with MA-471 resulted in "good" or "acceptable" control in over 68% of patients. MA-471 supplementation also resulted in a significant fall in serum total cholesterol and triglycerides, and resulted in marked improvement in polyuria, fatigue, and constipation. MA-471 seemed to be more effective in patients who had diabetes for less than five years.

Immunity Research

1. Title

Dose-Dependent Activation of Immune Function in Mice by Ingestion of Maharishi Amrit Kalash-5 (MAK-5)

Publication

Environmental Health and Preventive Medicine, Vol. 2, No. 1, pp. 35-39, 1997.

Authors

Ryoichi Inaba*, Haruo Sugiura*, Hirotoshi Iwata* and Takuji Tanaka**.

Conducted at

*Department of Hygiene, Gifu University School of Medicine, Gifu, Japan

**First Department of Pathology, Gifu University School of Medicine, Gifu, Japan.

Summary

This study evaluated the dose-effects of ingestion of Maharishi Amrit Kalash-5 (MAK-5), an Ayurvedic food supplement, on the immune function in 10-week female inbred BALB/c mice. Superoxide anion (O^2) production of peritoneal macrophages and the response of spleen cells to concanavalin A (Con A) were examined in mice given MAK-5 by gastric intubation of an aqueous emulsion at the doses of 10, 50, 100 and 200 mg/kg once a day for 20 days. Glucose consumption of peritoneal macrophages in the MAK-5-treated mice at all doses after 24 hours of incubation, and only at the dose of 200 mg/kg after 48 hours of incubation were significantly higher

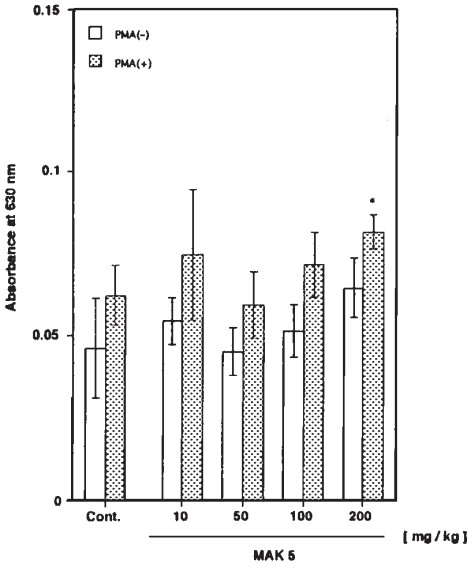

Fig. 2 Effects of Maharishi Amrit Kalash 5 (MAK 5) on superoxide anion (O_2^-) production of peritoneal macrophages in mice. Each value represents the mean±SE of triplicate determinations. *p<0.05, compared with the controls. Cont., Control.

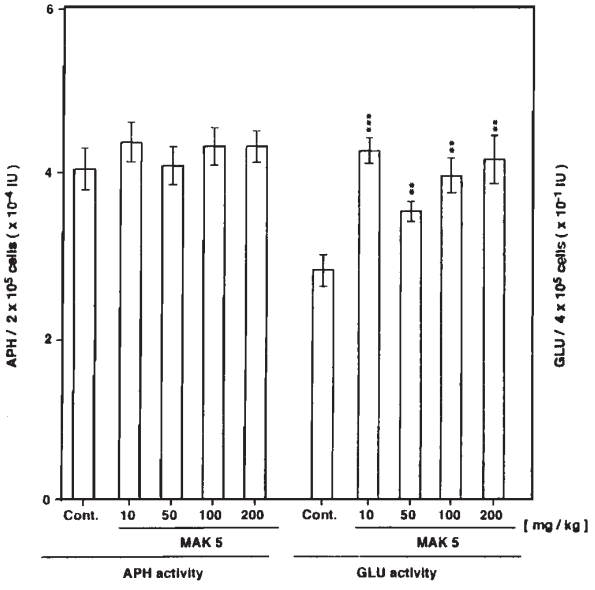

Fig. 3 Effects of Maharishi Amrit Kalash 5 (MAK 5) on acid phosphatase (APH) and β-glucuronidase (GLU) activities of peritoneal macrophages in mice. Each value represents the mean±SE of triplicate determinations. **p<0.01, ***p<0.001, compared with the controls. Cont., Control.

than those in the control group. O^{2}-production of peritoneal macrophages in the presence of stimulator was significantly higher in the MAK-5-treated group at the dose
of 200 mg/kg than in the control group. Activities of ß-glucuronidase and lactate dehydrogenase in the peritoneal macrophages were significantly increased in the MAK-5-treated mice at all doses. MAK-5 did not enhance spontaneous splenic lymphocyte proliferation at any dose in mice. Stimulation indices in the MAK 5-treated groups at the doses of 50, 100 and 200 mg/kg were significantly higher than that of the control group. These results indicate that gastric intubation of MAK-5 once a day at the dose of 50 mg/kg enhances not only macrophage function but also lymphocyte responsiveness in mice.

Dose-Effects of MAK 5 on Immune Function

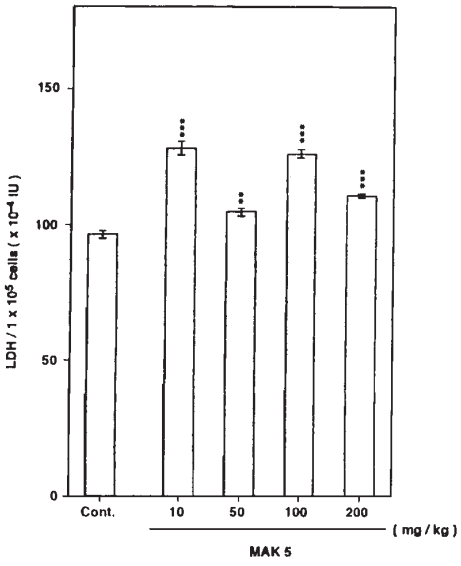

Fig. 4 Effects of Maharishi Amrit Kalash 5 (MAK 5) on lactate dehydrogenase (LDH) activities of peritoneal macrophages in mice. Each value represents the mean±SE of triplicate determinations.
** p<0.01, ***p<0.001, compared with the controls.
Cont., Control.

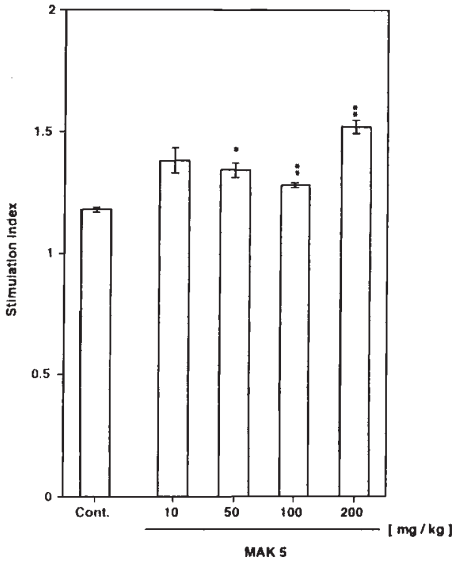

Fig. 5 Effects of Maharishi Amrit Kalash 5 (MAK 5) on proliferation of splenocytes induced by Con A in mice. Each value represents the mean±SE of 4 mice. *p<0.05, **p<0.01, compared with the controls. Cont., Control.

Study 1 **Research Highlights**
As demonstrated in mice, gastric intubation of MAK-5 once a day at the dose of 50 mg/kg enhanced not only macrophage function but also lymphocyte responsiveness.

2. Title

Immunomodulatory Effects of Maharishi Amrit Kalash 4 and 5 [MAK-4 and MAK-5] in Mice

Publication

Japan Journal of Hygiene, Vol. 50, No. 4, pp. 901-905, 1995.

Authors

Ryoichi Inaba, Haruo Sugiura, and Hirotoshi Iwata.

Conducted at

Gifu University School of Medicine, Department of Hygiene, Gifu 500, Japan

Summary

To evaluate the immunomodulatory effects of two kinds of Ayurvedic food supplements (Maharishi Amrit Kalash 4 and Maharishi Amrit Kalash 5, MAK-4 and MAK-5), superoxide anion production of peritoneal macrophages and the response of spleen cells to concanavalin A (Con A) were examined in mice given an aqueous emulsion of MAK-4 and MAK-5 p.o. at doses of 50 and 100 mg/kg for 10 days. Superoxide anion production of peritoneal macrophages in the MAK-5 (50 mg/kg)-treated group was significantly higher than that in the control group. The indices of stimulation of spleen cells by Con A were significantly (3 to 4 times) higher in groups treated with MAK-4 and MAK-5 at all doses than in the control group. These results indicate that MAK-4 enhances lymphocyte responsiveness and MAK-5 enhances not only lymphocyte responsiveness, but also macrophage function. It is also suggested in this study that MAK-4 and MAK-5 have mitogenic effects on lymphocytes.

Study 2 **Research Highlights**

As demonstrated in mice, MAK-4 enhances lymphocyte responsiveness, and MAK-5 enhances not only lymphocyte responsiveness, but also macrophage function. It also is suggested that MAK-4 and MAK-5 have mitogenic effects on lymphocytes.

Table 2 Effects of M-4 and M-5 on proliferation of splenocytes induced by Con A in mice.

Group	N	Absorbance (570 nm) Con A (−)	Con A (+)
Control	4	0.045 ±0.001	0.249 ±0.021
M-4			
50 mg/kg	4	0.088** ±0.004	0.800** ±0.019
100 mg/kg	4	0.075** ±0.001	0.744** ±0.015
M-5			
50 mg/kg	4	0.084** ±0.003	0.740** ±0.011
100 mg/kg	4	0.095** ±0.004	0.950** ±0.019

Each value represents the mean ±SE.
Significantly different from control at **$p<0.01$.
M-4, Maharishi Amrit Kalash 4; M-5, Maharishi Amrit Kalash 5. N, Number of mice used.

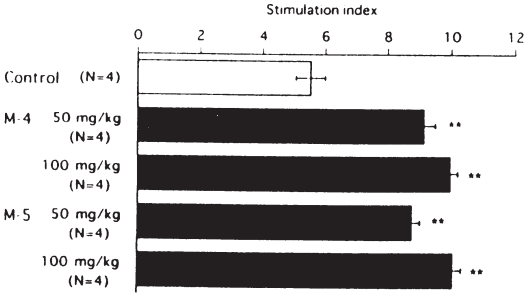

Fig. 2 Effects of M-4 and M-5 on proliferation of splenocytes induced by Con A in mice.
Each column and horizontal bar represents the mean ± SE.
Significantly different from control at ** $p<0.01$.
M-4, Maharishi Amrit Kalash 4; M-5, Maharishi Amrit Kalash 5. N, Number of mice used.

3. Title

Immunomodulation by Maharishi Amrit Kalash [MAK-4] in Mice

Publication

Journal of Applied Nutrition, Vol. 48, Nos. 1 and 2, pp. 10-21, 1996.

Authors

Ryoichi Inaba, PhD,* Haruo Sugiura, PhD,* Hirotoshi Iwata, PhD,* Hiroshi Mori, PhD,** and Takuji Tanaka, PhD.†

Conducted at

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Summary

The effects of ingestion of Maharishi Amrit Kalash-4 (MAK-4), one of the Ayurvedic food supplements, on immune function were evaluated in male A/He mice aged 7 weeks. Production of nitric oxide (NO) by peritoneal macrophages and proliferation of spleen cells stimulated by mitogens was examined in mice given MAK-4 by gastric intubation at the doses of 10, 50, and 100 mg/kg once a day for 20

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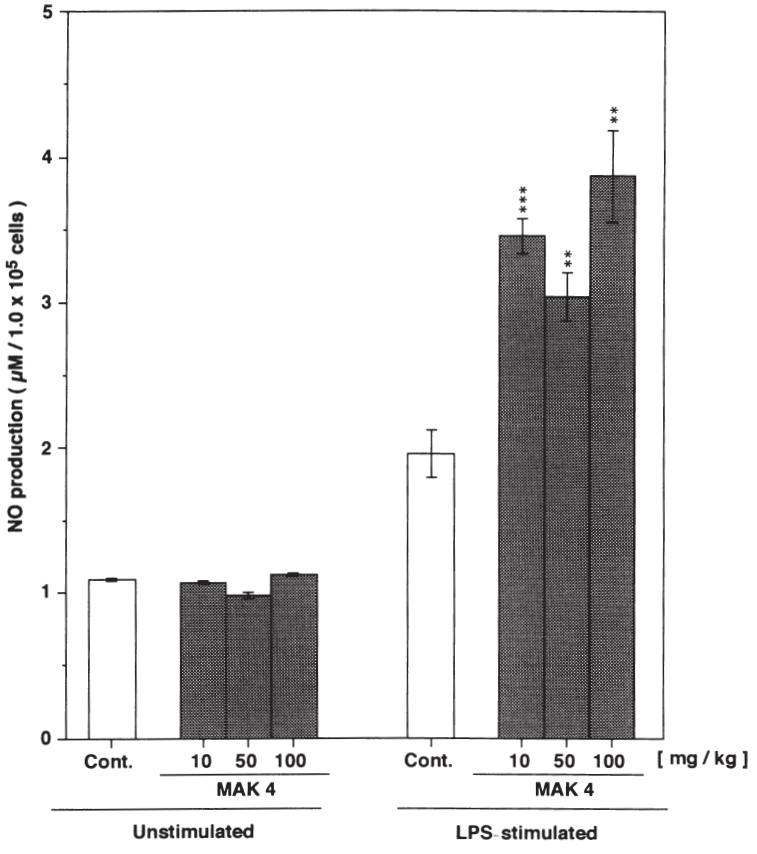
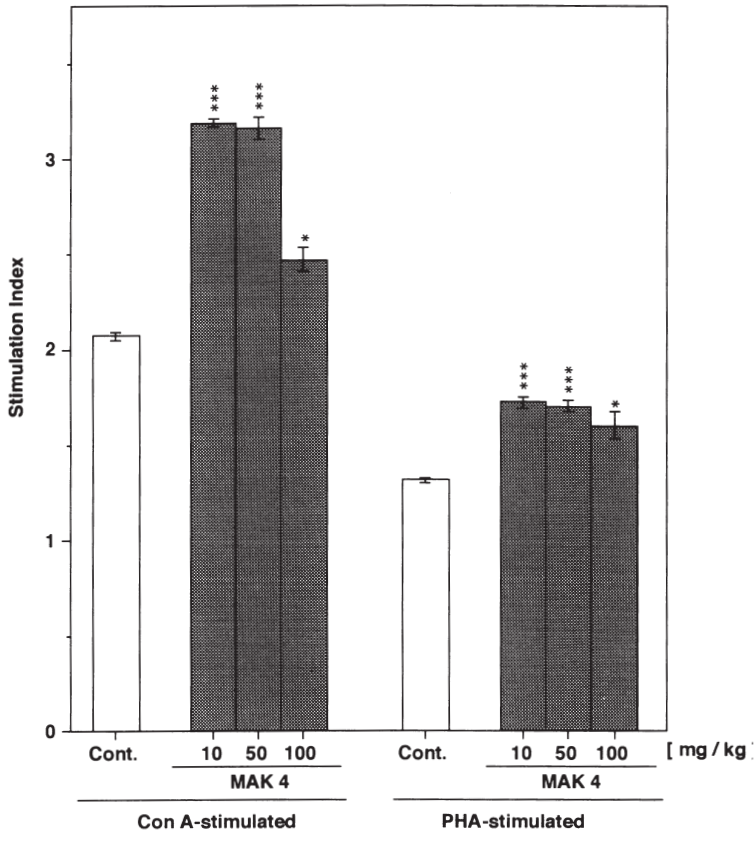
Figure 4 Effects of Maharishi Amrit Kalash 4 (MAK 4) on nitric oxide (NO) production by peritoneal macrophages cultured for 24 hours in mice.



Each value represents the mean ± SE of triplicate determinations. * $p<0.05$, * * $p<0.01$, * * * $p<0.001$, compared with the control group (Cont.). LPS, lipopolysaccharide.

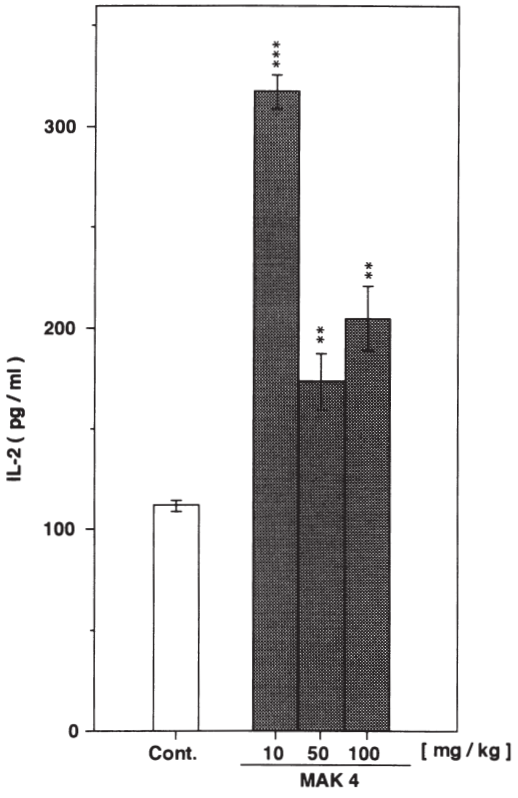
days. Glucose consumption of peritoneal macrophages during incubation up to 72 hours at all doses of MAK-4 was significantly higher in the MAK-4 treated mice than in the control group ($p < 0.05$). Activities of lactate dehydrogenase in the peritoneal macrophages were significantly increased in the MAK-4 treated mice at all doses ($p < 0.01$). Macrophage production of NO stimulated by lipopolysaccharide in the MAK-4 treated mice at all doses was significantly increased ($p < 0.01$). Stimulation indices both by concanavalin A (Con A) and phytohaemagglutinin in the MAK-4 treated groups at all doses were significantly higher than those of the control group ($p < 0.05$). Splenocyte production of interleukin-2 (IL-2) stimulated by Con A in the MAK-4 treated mice at all doses was significantly increased ($p<0.01$). MAK-4 treated mice at the dose of 10 mg/kg had the highest IL-2 production by splenocytes. MAK-4 at any of the doses used did not enhance spontaneous NO production, spontaneous splenic lymphocyte proliferation, or spontaneous IL-2 production by splenocytes. These results indicate that gastric intubation of MAK-4 once a day at a dose of 10 mg/kg or more enhances not only macrophage function but also lymphocyte responsiveness in mice.

Figure 5 Effects of Maharishi Amrit Kalash 4 (MAK 4) on concanavalin A (Con A) - and phytohaemagglutinin (PHA) - stimulated splenocytes proliferative responses in mice.



Each value represents the mean ± SE of 4 mice. * p<0.05, * * p<0.01, * * * p<0.001, compared with the control group (Cont.).

Figure 6 Effects of Maharishi Amrit Kalash 4 (MAK 4) on concanavalin A (Con A) – stimulated splenocyte production of interleukin-2 (IL-2) in mice.



Each value represents the mean ± SE of mice. * * p<0.01, * * * p<0.001, compare with the control group (Cont.).

Study 3 **Research Highlights**
MAK-4 once a day at a dose of 10 mg/kg or more enhances not only macrophage function but also lymphocyte responsiveness in mice.

4. Title

Enhanced Lymphoproliferative Response, Macrophage-Mediated Tumor Cell Killing and Nitric Oxide Production After Ingestion of an Ayurvedic Drug [MAK-5].

Publication

Biochemical Archives, Vol. 9, pp. 365-374, 1993.

Authors

Kottarappat N. Dileepan, Sapna T. Varghese, Jordan C. Page, and Daniel J. Stechschulte.

Conducted at

Division of Allergy, Clinical Immunology and Rheumatology, Department of Medicine, University of Kansas Medical Center, Kansas City, KS 66160

Summary

The Ayurvedic system of medicine utilizes a variety of herbal food supplements to enhance the body's resistance to infection and disease. Maharishi Amrit Kalash Ambrosia (MAK-5) is one such commercially available food supplement. In order to evaluate its potential immunomodulatory actions, we studied the effect of ingestion of MAK-5 on lymphoproliferative response, macrophage-mediated tumor cell killing, and the production of nitric oxide (NO) by macrophages. C57BL/6J mice were fed either a standard diet or that supplemented with 0.3% MAK-5, for a period of six weeks. After this time, splenic lymphocytes and peritoneal macrophages were isolated. The lymphoproliferative response was measured by [^{3}H] thymidine uptake after activation of the lymphocytes with phytohemagglutinin (PHA) or anti-CD3 antibodies. Tumor cell killing by lipopolysaccharide (LPS)- or interferon (IFN)-activated macrophages was studied by an 18-hour [^{51}Cr] release assay using P815 murine mastocytoma cells as targets. Production of NO was assayed by measuring the nitrite contents in the 24-hour culture supernatants of macrophage monolayers activated with IFN or a combination of LPS and IFN. In comparison to controls, lymphocytes from mice fed the MAK-5-supplemented diet exhibited significantly higher proliferative responses to PHA and anti-CD3 at all concentrations tested. The spontaneous rate of lymphocyte proliferation, measured in the absence of activators, was not enhanced by the MAK-5 diet. Peritoneal macrophages from mice maintained on the MAK-5-supplemented diet demonstrated enhanced tumor cell killing when activated with LPS, IFN, or LPS plus IFN. The production of NO by LPS- or IFN-activated macrophages from MAK-5 treated mice was significantly higher than those from controls. Neither the cytotoxicity nor the production of NO by unactivated macrophages was altered by MAK-5 supplementation. These results indicate that MAK-5 contains ingredients that can induce in vivo priming of both T-cells and macrophages for enhanced functions.

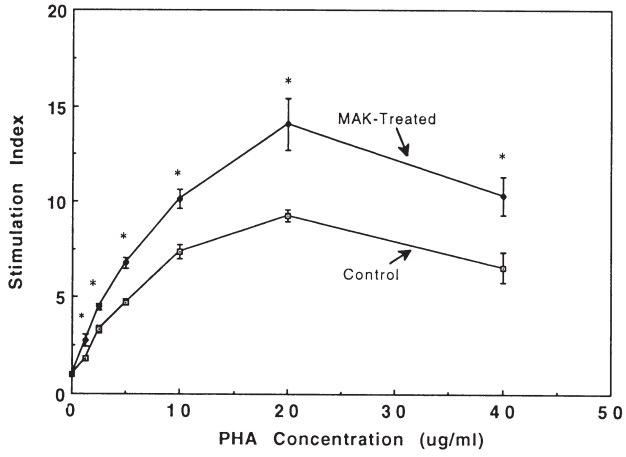


Figure 1. Effect of MAK treatment on PHA-induced splenic lymphocyte proliferation. The lymphoproliferative response to PHA was determined by the in vitro [^{3}H]-thymidine uptake assay as described. Stimulation index is the ratio of PHA-induced [^{3}H]-thymidine uptake to the unstimulated basal uptake. Each value given is the mean ± SEM of quadruplicate determinations. The results presented here are from a typical experiment using pooled splenic lymphocytes. A similar effect of MAK on PHA-induced lymphocyte proliferation has been noted in another experiment with a different batch of MAK. *This indicates statistically significant at least at $p<0.05$.

(continued)

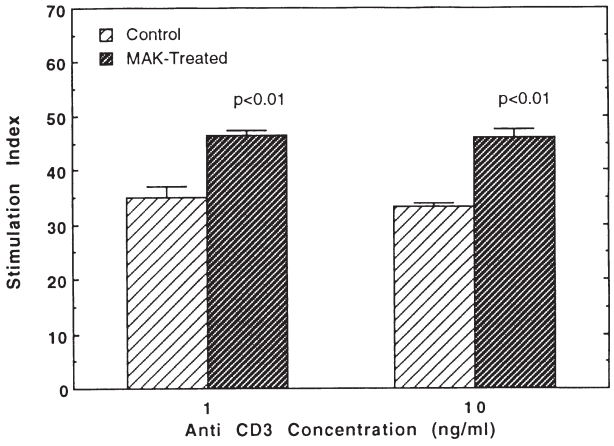


Figure 2. Effect of MAK treatment on anti CD3-induced splenic lymphocyte proliferation. The lymphoproliferative response to anti-CD3 was determined by the in vitro ^{3}H-thymidine uptake assay as described. Stimulation index is the ratio of anti-CD3-induced ^{3}H-thymidine uptake to the unstimulated basal uptake. Each value given is the mean ± SEM of quadruplicate determinations.

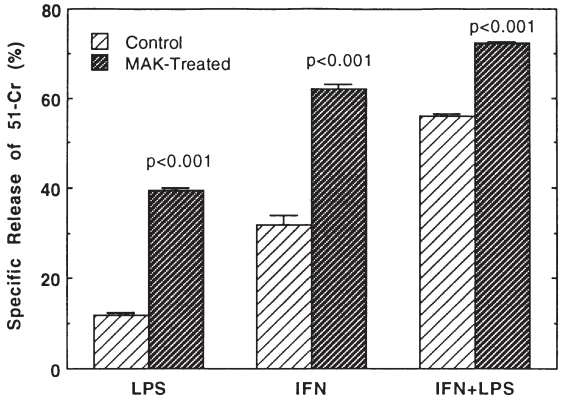


Figure 3. Effect of MAK treatment on macrophage-mediated tumor cell killing. Macrophage-mediated tumor cell killing was assayed by monitoring the release of ^{51}Cr from radiolabeled P815 mastocytoma cells (tumor targets) in an 18 hour co-culture. Concentrations of the activators used were: LPS, 1 μg/ml; IFN$_{\gamma}$, 100 units/ml. Each value given is mean ± SEM of triplicate determinations.

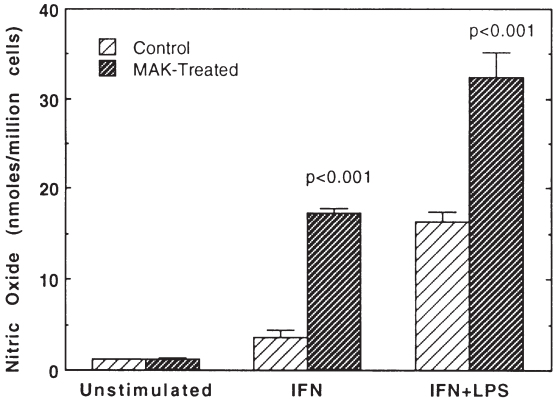


Figure 4. Effect of MAK treatment on nitric oxide production by macrophages. Production of nitric oxide by macrophages was assayed by monitoring nitrite content in the culture supernatants after 24 hour culture. Concentrations of the activators used were: LPS, 1 μg/ml; IFN$_{\gamma}$, 100 units/ml. Each value given is mean ± SEM of quadruplicate determinations.

Study 4 **Research Highlights**

As tested in splenic lymphocytes and peritoneal macrophages isolated from mice fed MAK-5 for six weeks, MAK-5 seems to contain ingredients that can induce in vivo priming of both T-cells and macrophages for enhanced functions.

5. Title

Priming of Splenic Lymphocytes After Ingestion of an Ayurvedic Herbal Food Supplement [MAK-5]: Evidence for an Immunomodulatory Effect

Publication

Biochemical Archives, Vol. 6, pp. 267-274, 1990.

Authors

Kottarappat N. Dileepan,* Vimal Patel,** Hari M. Sharma,† and Daniel J. Stechschulte.*

Conducted at

* Division of Allergy, Clinical Immunology and Rheumatology, Department of Medicine, University of Kansas Medical Center, Kansas City, KS 66103

**Department of Pathology, Indiana University School of Medicine, Indianapolis, IN 46223

† Department of Pathology, Ohio State University College of Medicine, Columbus, OH 43210

Summary

The in vivo immunomodulatory effects of an Ayurvedic food supplement (Maharishi Amrit Kalash Ambrosia, MAK-5) were studied in rats gavaged with this preparation at a dose of 50 mg/day for 10 or 20 days. After these regimens, mitogen-induced lymphocyte proliferation, macrophage superoxide anion production, and phagocytosis were assayed. In vitro lymphoproliferative responses to various mitogens were markedly enhanced by MAK-5 ingestion. MAK-5-mediated increases in stimulation indices ranged from 32-88% for varying concentrations of phytohemagglutinin (PHA). MAK-5 treatment did not affect spontaneous lymphocyte proliferation. The lymphoproliferative response induced by MAK-5 ingestion was significant even in animals treated for 10 days and persisted for at least 15 days after discontinuation of MAK-5. Macrophage superoxide anion generation and phagocytosis were unaltered as a result of MAK-5 treatment. These data indicate that ingestion of this food supplement enhances lymphocyte responsiveness to mitogens without affecting spontaneous proliferation.

Study 5 **Research Highlights**

As evaluated in mice, MAK-5 enhances lymphocyte responsiveness to mitogens without affecting spontaneous proliferation.

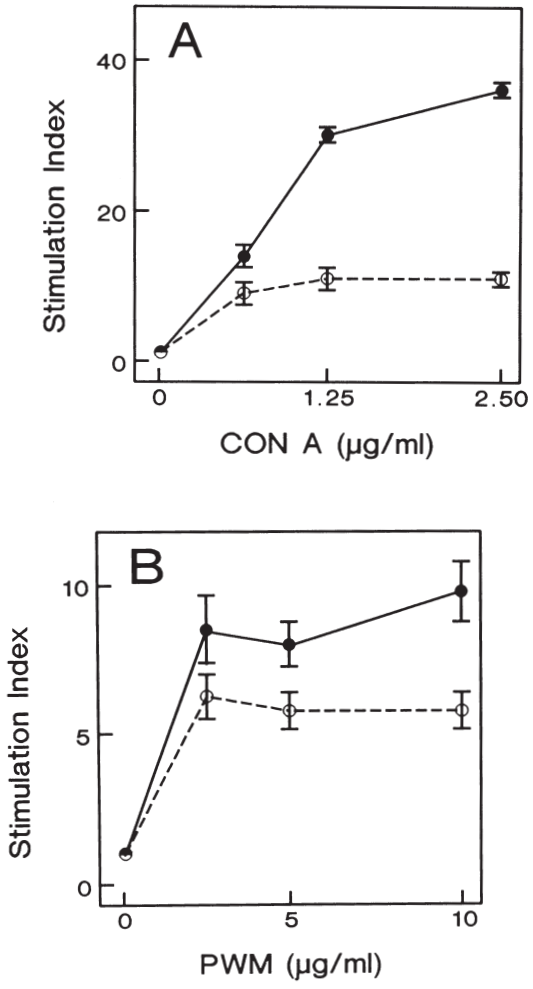


Figure 1

Proliferative response of splenic lymphocytes from control (o-o) and MAK-treated (•-•) rats to Con A (Panel A) and pokeweed mitogen (Panel B).

Research on Anti-Aging, Neurophysiology and Intelligence

1. **Title**

The Effect of the Maharishi Student Rasayana Food Supplement on Non-Verbal Intelligence

Publication

Personality and Individual Differences, Vol. 15, No. 5, pp. 599-602, 1993.

Authors

Sanford I. Nidich,* Paul Morehead,* Randi J. Nidich,* David Sands,** and Hari Sharma.†

Conducted at

* Department of Science of Creative Intelligence and Education, and
**Department of Physiological and Biological Sciences, Maharishi International University, Fairfield, IA 52556
† The Ohio State University, College of Medicine, Columbus, OH

Summary

Research shows that IQ is a strong predictor of student academic performance. Previous studies have found that increasing the intake of vitamins and minerals improves non-verbal intelligence. The purpose of this study was to measure the effect of an herbal food supplement, Maharishi Ayur-Veda Student Rasayana (MA-SR), on non-verbal intelligence. The 5-month study consisted of 34 third-grade students who were randomly assigned to either an experimental group or a placebo group. The MA-SR group exhibited a 9.83 point increase in IQ compared to 4.88 points for the placebo group. Analysis of the data indicated that a significant proportion of students in the MA-SR group (78%) compared to that of the placebo group (50%) showed an improvement in IQ which exceeded that of the test-retest effect. Additional statistical analysis further indicated that taking MA-SR improves IQ.

Table 3. Mean changes in IQ for matched MA-SR and placebo groups ($N = 28$)

		Pretest		Posttest		Change	
Groups	N	M	SD	M	SD	M	SD
Rasayana	14	118.57	8.03	125.86	9.95	7.29*	6.01
Placebo	14	121.64	7.65	123.36	11.05	1.71**	11.41

*$F(1,13) = 20.573$, $P < 0.001$, repeated measures on MA-SR group pretest/posttest scores; **$F(1,13) = 0.213$, $P = 0.328$, NS, repeated measures on placebo pretest/posttest scores.

Study 1 **Research Highlights**

2. A significant portion (78%) of third-grade students taking Maharishi Student Rasayana (MA-SR) Food Supplement showed an improvement in IQ that exceeded that of the test-retest effect, as compared to the placebo group. Additional statistical analysis further indicated that taking MA-SR improves IQ.

Title

Effect of Herbal Mixture Student Rasayana on Lipoxygenase Activity and Lipid Peroxidation

Publication

Free Radical Biology and Medicine, Vol. 18, No. 4, pp. 687-697, 1995.

Authors

Hari M. Sharma, Atef N. Hanna, Ellen M. Kauffman, and Howard A.I. Newman.

Conducted at

Department of Pathology, College of Medicine, The Ohio State University, Columbus, OH

Summary

There is evidence that suggests a relationship among free radicals, brain injury, and brain functionality. The scavenging of free radicals as a possible mechanism for the improvement in intelligence by Student Rasayana (SR) was explored in this study on the effect of SR on lipid peroxidation and lipoxygenase activity. SR inhibited enzymatic- and nonenzymatic-induced rat liver microsomal lipid peroxidation in a concentration-dependent manner ($p<0.05$). SR also inhibited soyabean lipoxygenase-induced LDL oxidation in vitro ($p<0.05$). In vivo, SR inhibited toluene-induced rat brain microsomal lipid peroxidation ($p<0.05$). An interesting finding in this study is that an alcoholic extract of SR increased in vitro a metabolite of arachidonic acid which enhances long-term potentiation, a process associated with learning. Thus, SR may protect brain functions and increase intelligence through scavenging of free radicals and/or increasing certain metabolites of arachidonic acid.

For more information on this study, see Research on Reduction of Chemical Toxicity and Antioxidant Research.

Study 2 **Research Highlights**
An alcoholic extract of Student Rasayana (SR) increased a metabolite of arachidonic acid, which enhances long-term potentiation, a process associated with learning. Thus, SR may protect brain functions and increase intelligence through scavenging of free radicals and/or increasing certain metabolites of arachidonic acid.

3. Title

In Vivo Effect of Herbal Mixture MAK-4 on Antioxidant Capacity of Brain Microsomes

Publication

Biochemical Archives, Vol. 12, pp. 181-186, 1996.

Authors

Hari M. Sharma, Jae Y. Lee, Ellen M. Kauffman, and Atef N. Hanna.

Conducted at

Department of Pathology, College of Medicine, The Ohio State University, Columbus, OH 43210

Summary

There is increasing evidence that free radicals are linked to neurological disorders and aging. This study examined the in vivo effect of MAK-4 on lipid peroxidation and antioxidant protection capacity of the brain of Watanabe Heritable Hyperlipidemic (WHHL) rabbits. Brain microsomes of rabbits fed MAK-4 showed significantly lower levels of lipid peroxidation than those of control rabbits fed normal chow. These results indicate MAK-4 may yield increased antioxidant protection in the brain, and may therefore be useful in preventing or treating free radical-induced neurological disorders.

For details of this study, see Antioxidant Research.

Study 3 **Research Highlights**
Research with Watanabe Heritable Hyperlipidemic rabbits suggests that MAK-4 may yield increased antioxidant protection in the brain, and may therefore be useful in preventing or treating free radical-induced neurological disorders.

4. Title

Antioxidant Properties of Two Ayurvedic Herbal Preparations [MAK-4 and MAK-5]

Publication

Biochemical Archives, Vol. 10, pp. 25-31, 1994.

Authors

Stephen C. Bondy, Tina M. Hernandez, and Cara Mattia.

Conducted at

Department of Community and Environmental Medicine, University of California (Irvine), Irvine, CA 92717

Summary

This study investigated the antioxidant effects of MAK-4 and MAK-5 in the rat brain in vitro and in vivo. In vitro, ethanol and aqueous extracts of MAK-4 and MAK-5 were able to quench generation of reactive oxygen species within an isolated fraction of rat cerebral cortex enriched in mitochondria and nerve endings (synaptosomes). In vivo, the excess production of reactive oxygen species observed within the cerebellar mitochondrial fraction after exposure of rats to toluene, was prevented by pretreatment with MAK-5.

For more information on this study, see Research on Reduction of Chemical Toxicity and Antioxidant Research.

Study 4 **Research Highlights**
In vivo and in vitro studies showed that MAK-4 and MAK-5 were able to quench the excess generation of reactive oxygen species in rat brains.

5. Title

Effect of Maharishi Amrit Kalash [MAK-5] on Brain Opioid Receptors and Neuropeptides

Publication

The Journal of Research and Education in Indian Medicine, Vol. 10, No. 1, pp. 1-8, 1991.

Authors

Hari M. Sharma,* Silva Hanissian,** Anil K. Rattan,** Stephen L. Stern,† and Gopi A. Tejwani.**

Conducted at

*Department of Pathology, **Department of Pharmacology, and †Division of Psychiatry, College of Medicine, The Ohio State University, Columbus, OH 43210

Summary

MAK-5 was tested for its effects on opioid receptors in the brain, and on neuropeptides. In vitro tests using animal brain tissue showed that MAK-5 inhibited the binding of mu, kappa, and delta opioid receptors. Opioid peptides binding to these receptors are known to trigger changes in analgesia, behavior, appetite, endocrine and autonomic functions, and modulation of the immune system. Levels of Substance P, a neurotransmitter involved in pain pathways

Table 2 Effect of MAK on Plasma Neuro peptides and Cortisol in Human Subjects.

	Before MAK*	After MAK*
Prolactin (ng/ml)	4.2 ± 0.50 (8)	4.0 ± 0.46 (8)
Substance P (pg/ml)	255.8 ± 70.0 (5)	36.0 ± 9.7** (7)
VIP (pg/ml)	43.5 ± 13.1 (8)	42.5 ± 12.5 (8)
Somatostatin (pg/ml)	34.0 ± 2.7 (8)	31.0 ± 0.0 (8)
Cortisol (μg/dl)	12.4 ± 1.6 (8)	12.3 ± 1.2 (8)

* Values are Mean ± SEM and number of observations are in parentheses.
** Value is significantly different from the value before MAK ingestion.

and pulmonary and gastrointestinal inflammation, showed a significant decrease in human subjects using MAK-5 for three months. Levels decreased from 255.8 pg/ml to 36.0 pg/ml over the 3-month period ($p<0.01$). This suggests MAK-5 may be helpful in relieving pain, as well as pulmonary and gastrointestinal inflammation.

Study 5 **Research Highlights**
In vitro tests using animal brain tissue and human studies measuring neurotransmitter levels associated with pain, suggest that MAK-5 may be helpful in relieving pain, as well as pulmonary and gastrointestinal inflammation.

6. Title
Influence of a Maharishi Ayur-Vedic Herbal Preparation [MAK-5] on Age-Related Visual Discrimination

Publication
International Journal of Psychosomatics, Vol. 37, Nos. 1-4, pp. 25-29, 1990.

Authors
P. Gelderloos, SScD, H.H.B. Ahlstrom, MS, D.W. Orme-Johnson, PhD, D.K. Robinson, MS, R.K. Wallace, PhD, and J.L. Glaser, MD.

Conducted at
Maharishi University of Management, Fairfield, IA

Summary
An ancient system of natural medicine—Maharishi Ayur-Veda—prescribes certain herbal formulas to enhance cognitive functioning, prevent illness, and alleviate the detrimental effects of the aging process. A double-blind study was conducted to test the effect of an Ayurvedic herbal preparation, Maharishi Amrit Kalash (MAK-5), on an age-related alertness task. Forty-eight men over 35 years of age were randomly assigned to receive MAK-5 tablets or a closely matched placebo twice daily for six weeks. A visual discrimination task consisted of the identification of the exact location of a stimulus "v" within an array of "x" symbols in tachistoscopic presentations. The MAK-5 group improved significantly more in their performance of this task after three and six weeks of treatment relative to the placebo group. Performance was highly correlated with age, and because successful performance apparently requires an unrestricted flow of homogeneous attention as well as focalized concentration, it is concluded that MAK-5 may enhance attentional capacity or alertness, and thus reverse some of the detrimental cognitive effects of aging.

Study 6 **Research Highlights**
A group of men over 35 years of age and supplemented with MAK-5 twice daily for six weeks, showed a significant improvement in a visual discrimination task as compared with a placebo group. Performance was highly correlated with age. MAK-5 may enhance attentional capacity or alertness, and thus reverse some of the detrimental cognitive effects of aging.

7. Title

Anti-Aging Effect of a Natural Product, Maharishi Amrit Kalash (MAK)

Presented at

Joint Meeting of the International Union of Biochemists – Symposium No. 200, Satellite Meeting of the Oxygen Society, and the International Society for Free Radical Research, Berkeley, CA, January 26-27, 1990.

Authors

J.Z. Fields,* R.H. Schneider,** L. Wichlinski,* and J. Hagen.*

Conducted at

* Department of Pharmacology, Hines V.A. – Loyola University Medical Center, Maywood, IL

** Department of Physiology, Maharishi International University, Fairfield, IA

Summary

Aging is a concept that is not clearly defined. Is it the genetically coded final stage in development or the random accumulation of errors? Operationally, aging is seen as a process that increases susceptibility to disease and dysfunction. Interventions to retard or reverse this process would decrease disease, improve human function, and thereby increase quality of life and at least mean survival time.

Ayurvedic medicine, the traditional medicine of India, holds that Maharishi Amrit Kalash (MAK) has substantial anti-aging properties. Accordingly, we studied the effects of this novel herbal preparation, MAK, on aging and related parameters. MAK is a combination of 26 plants (Maharishi Ayurveda Products International, Stoneham, Massachusetts).

Fifty-eight C57BL/6 mice (males) started on dietary MAK supplements at 25 mo, and kept on them for up to 8 weeks, showed significantly ($p < 0.05$) more activity (locomotion, +85%), more coordination (roto-rod, +23%) and lower heart weight (-30%).

For mice ($n = 58$) started at 18 mo, 80% of MAK mice were alive at 23 mo vs. 48% for controls ($p < 0.05$). In these survivors, body weights for controls (41.5 g) and for MAK mice (38.3 g) were not significantly different.

MAK also increased acute survival 7 days after injection of a cytotoxic drug mitomycin-c at 3.25 mg/kg: 100% of MAK (Fisher female) rats (9 of 9) were alive compared to 33% (2 out of 6) for controls ($p<0.05$).

The finding of H. Sharma (Physiol. Biochem. Behav., in press) that MAK prevents cancer also suggests an anti-aging effect. The anti-aging mechanism(s) may include scavenging of reactive oxygen metabolites (ROM) by low molecular weight anti-oxidants. Using aqueous extracts, we found that MAK was as competent as superoxide dismutase (100% inhibition) and as potent, mg for mg, at scavenging one oxygen free radical, superoxide anions, produced by human neutrophils (PMN) (reduction of ferricytochrome-c assay). In vitro, at similar MAK concentrations, hypochlorous acid (HOCl) was also scavenged (iodometric assay). HOCl is another PMN-generated ROM and may be even more directly involved in tissue injury.

The maximum anti-aging effects of MAK, the full effects in man, and the active ingredients of MAK and their mechanisms remain to be determined.

Study 7 **Research Highlights**

MAK supplementation to mice at 18 mo and continuing to 23 mo showed increased survival rates as compared with controls. Mice started on dietary MAK supplements at 25 mo and continuing for 8 weeks showed significantly more activity, more coordination and lower heart weight. MAK also significantly increased acute survival of rats 7 days after injection of a cytotoxic drug.

8. Title

Maharishi Amrit Kalash [MAK-4 and MAK-5] Rejuvenates Ageing Central Nervous System's Antioxidant Defense System: An *In Vivo* Study

Publication

Pharmacological Research, Vol. 40, No. 6, pp 497-502, 1999.

Authors

Bhupinder Pal Singh Vohra,* Satya Prakash Sharma,* and Vinod Kumar Kansal.**

Conducted at

* Laboratory of Nutritional Histopathology and Ageing, Department of Zoology, Kurukshetra University, Kurukshetra—136 119, Haryana, India

**Animal Biochemistry Division, National Dairy Research Institute, Karnal, Haryana, India

Summary

The oxygen-free radical involvement in various deteriorative processes and in aging is unquestionably established. In the present study, age-related changes in antioxidant enzyme activity in the different regions of CNS of 10-month and 32-month-old guinea pigs were studied. Maharishi Amrit Kalash has shown promise in inhibiting the in vitro and in vivo lipid peroxidation. Therefore, in the present study the effect of MAK on the activity of antioxidant enzymes was checked. Our results indicate that the activity of superoxide dismutase and glutathione peroxidase, was found to be reduced $p<0.05$ in all the regions of CNS studied. The activities of catalase declined significantly only in the cerebral cortex, hypothalamus and the cerebellum, whereas glutathione reductase activity declined in the cerebral cortex and hypothalamus. It is concluded that the age-related decline in the activities of antioxidant enzymes is region-specific as well as enzyme-specific. The endogenous lipid peroxide was found to be increased significantly $p<0.05$ in the 32-month old animals, whereas the lipid peroxidation after incubating the tissue homogenate in the air was found to be decreased $p<0.05$ in the older animals. The results indicate that the accumulation of lipid peroxides takes place with age, but the susceptibility of lipid peroxidation decreases in the older animals. The treatment of MAK 500 mg kg^{-1} body wt for 2 months could augment the activities of antioxidant enzymes $p<0.05$. The effect of MAK was more pronounced in older than younger animals. It is concluded that the MAK can be used in compensating the decline in the activities of antioxidant enzymes in CNS, and thereby it reduces the risks of lipid peroxidation.

For more information on this study, see Antioxidant Research.

Study 8 **Research Highlights**

As demonstrated in guinea pigs, the treatment of MAK 500 mg/kg body wt for two months could augment the activities of antioxidant enzymes. Therefore, MAK could be used in compensating the decline in the activities of antioxidant enzymes in the CNS, thereby reducing the risks of lipid peroxidation.

9. Title

Effect of Maharishi Amrit Kalash, an Ayurvedic Herbal Mixture, on Lipid Peroxidation and Neuronal Lipofuscin Accumulation in Ageing Guinea Pig Brain

Publication

Indian Journal of Experimental Biology, Vol. 39, No. 4, pp. 355-359, 2001.

Authors

B.P. Vohra, S.P. Sharma, V.K. Kansal, and S.K. Gupta.

Conducted at

Laboratory of Nutritional Histopathology, Kurukshetra University, India

Summary

The effects of Ayurvedic herbal mixture Maharishi Amrit Kalash (MAK) were studied on brain lipid peroxidation, oxygen consumption, and lipofuscin accumulation in 10-month-old and 32-month-old guinea pigs. Brain regions studied were cerebral cortex, hypothalamus, cerebellum and spinal cord. Parameters assessed were lipid peroxidation, oxygen consumption, and lipofuscin accumulation. The endogenous lipid peroxide was found to be increased significantly ($p<0.05$) in the 32-month-old animals. Neuronal lipofuscin accumulation in the neurons of cerebral motor cortex, cerebellum and cervical spinal cord was increased ($p<0.05$) in the older animals. Oxygen consumption was found to be decreased significantly ($p<0.05$) in the 32-month-old guinea pigs. Treatment with MAK at a dose of 500 mg/kg body weight daily for two months reduced the lipid peroxidation and lipofuscin pigment accumulation significantly in brain regions, and it also helped in restoring the normal oxygen consumption in the older animals. This indicates antioxidant properties of MAK.

Study 9 **Research Highlights**

Treating guinea pigs with MAK at a dose of 500 mg/kg body weight daily for two months reduced lipid peroxidation in brain regions and helped restore normal oxygen consumption in older animals. This indicates antioxidant properties of MAK.

10. Title

Anti-Aging and Oxygen Free Radical (OFR) Scavenging Effects of an Anti-Carcinogenic Natural Product,

Maharishi Amrit Kalash [MAK-4 and MAK-5]

Publication

Federation of American Societies for Experimental Biology Journal, Vol. 5, No. 6, p. A1735, 1991 (Abstract).

Authors

J.Z. Fields, E. Eftekhari, J.F. Hagen, L.J. Wichlinski, and R.H. Schneider (SPON: A.H. Friedman).

Conducted at

Research Service 151, VA Hosp., Hines, IL 60141
Dept. of Pharmacology, Loyola Univ. Med. Sch., Maywood, IL
Dept. of Physiology, Maharishi International University, Fairfield, IA

Summary

MAK is an herbal preparation available as a food supplement. It is being taken for its anticipated health-promoting and anti-aging benefits. MAK refers to the combination of two natural products: M4 a paste, and M5 a tablet. Combined, MAK is comprised of plants or plant parts from 24 different herbs. Sharma et al. (Pharmacol Biochem Behav, 35:767–773, 1990) showed that MAK prevents and even reverses chemically induced breast tumors in rats. We showed (JZ Fields et al, The Pharmacologist, 32:155, 1990) that aqueous extracts of MAK scavenged both OFR (superoxide) and non-radical oxidants (hypochlorous acid) in suspensions of human neutrophils without compromising the viability of the cells. In mice (C57BL/6 male, $n = 29$/group) fed 6% MAK in the diet starting at 18 months of age, 80% of MAK mice were alive at 23 mo vs. 48% for controls ($p < 0.05$). Body weights for control (41.5 g) and MAK mice (38.3 g) were not significantly different. In fruitflies (male, wild type, Drosophila melanogaster, $n = 100$/group) fed 12% MAK from hatching to expiration, mean life span was significantly increased (+70%). The antioxidant properties and
anti-carcinogenic properties of MAK may contribute to its anti-aging properties.

Study 10 **Research Highlights**
Studies have been conducted in animals and in vitro demonstrating the antioxidant properties and anti-carcinogenic properties of MAK, which may contribute to its anti-aging properties.

Nutrition Insights

1. **Title**
   Nutritional Insights From Maharishi Ayur-Veda

Publication
Journal of Applied Nutrition, Vol. 48, Nos. 1 and 2, pp. 34-41, 1996.

Author
Hari M. Sharma, MD, FRCPC.

Conducted at
College of Medicine, The Ohio State University, Columbus, OH 43210

Summary

Major changes are needed in the health care arena to solve the current health care crisis. With the growing emphasis on prevention of disease, nutritional science can be a major part of these changes. However, a new paradigm is needed to address individual metabolic differences and seasonal variations in dietary needs. Maharishi Ayur-Veda (MAV), a comprehensive system of natural health care, provides this paradigm. MAV addresses differences in individual physiological functioning (Prakriti) and imbalances in the physiology (Vikriti). MAV considers taste and quality to be central features in the classification of foods, and seasonal factors as crucial in determining nutritional needs. MAV also advises use of certain herbal nutritional supplements to maintain optimum health. These supplements are rich in antioxidants and have been researched extensively for their health-promotion and disease-prevention properties. This new paradigm may enable nutritional science to play a major role in producing a renewed, healthy society.

Study 1 **Research Highlights**
A new paradigm is needed to address individual metabolic differences and seasonal variations in dietary needs. Maharishi Ayurveda addresses differences in individual physiological functioning and imbalances in the physiology and considers taste and quality to be central features in the classification of foods.

Research on Chronic Diseases

1. **Title**
The Maharishi Ayur-Veda Treatment of Ten Chronic Diseases—A Pilot Study

Publication
Netherlands Magazine of Integrated Science, Vol. 5, No. 35, pp. 586-594, 1989.

Author
G.W.H.M. Janssen, MD.

Conducted at
Maharishi Ayur-Veda Health Centre, Laag Soeren, The Netherlands

Summary
From September 1987 to January 1988, a preliminary research study was conducted in the Maharishi Ayur-Veda Health Centre at Laag Soeren on the effectiveness of the Maharishi Ayur-Veda treatments of the following diseases:

- rheumatoid arthritis
- bronchial asthma
- chronic bronchitis
- eczema
- psoriasis
- hypertension
- chronic constipation
- headache
- chronic sinusitis
- non-insulin-dependent diabetes mellitus

A total of 126 patients completed the treatment, which consisted of the following: diet program, Maharishi Ayur-Veda herbal preparations, and regulations for the daily routine. The patients could also make use of the following treatment procedures: physiological purification therapy, neuromuscular integration therapy, marma therapy, and the Transcendental Meditation technique for the development of consciousness.

Of the 126 patients, 100 (79%) experienced an improvement, 17 (14%) showed no change, and 9 (7%) experienced a worsening of their condition. The majority of the ten clinical conditions showed a significant or strongly significant improvement: rheumatoid arthritis ($p=0.04$), bronchial asthma ($p=0.09$), eczema ($p=0.03$), hypertension (diastolic blood pressure, $p=0.07$), chronic constipation ($p=0.0001$), headache ($p<0.0001$), and chronic sinusitis ($p=0.01$).

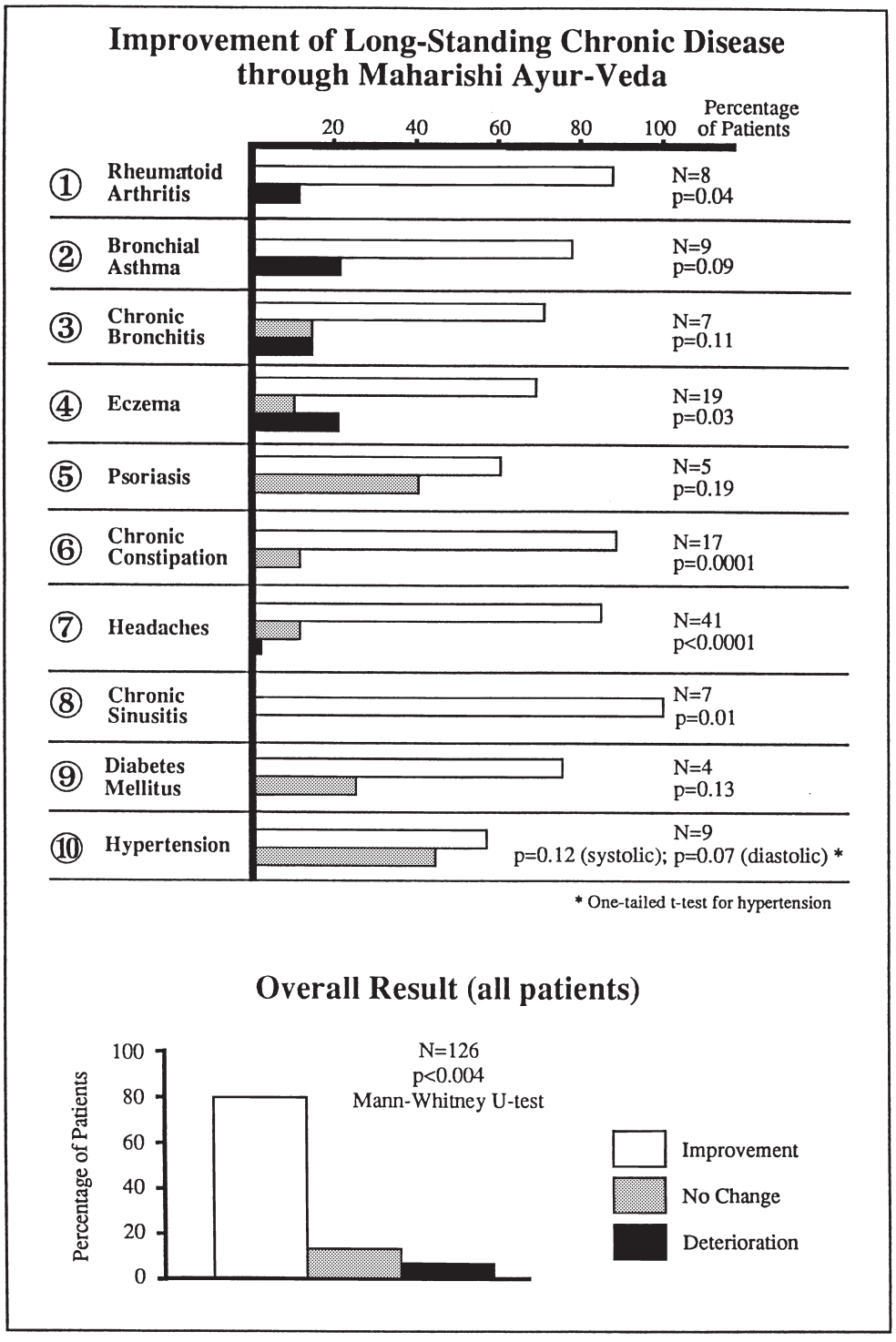
The following diseases showed a result in the predicted direction: chronic bronchitis ($p=0.11$), psoriasis ($p=0.19$), diabetes mellitus ($p=0.13$), and hypertension (systolic blood pressure, $p=0.12$).

Ten subjects could be declared cured during the research period. Of the 35 participants who had medication prescribed by their family doctor or specialist, 14 (40%) could reduce their dose or could even stop the medication. The Maharishi Ayur-Veda preparations were tolerated well by 95% of the patients.

On the basis of this research, it can be concluded that within a relatively short time the Maharishi Ayur-Veda treatment is able to bring about a substantial improvement in seven of the ten above-mentioned diseases, even if these have already existed for many years. It has been found that this form of therapy can be combined with other forms of treatment without any problem.

Considering the great number of patients suffering from chronic diseases and the results of treatment of these diseases with western medicine so far, and considering the effectiveness, lack of harmful side effects, and relatively low cost of Maharishi Ayur-Veda treatments, it is clear on the basis of the results of this study that the direct application of Maharishi Ayur-Veda is justifiable and desirable, and that further research into this treatment modality deserves the highest priority.

FIGURE 1



Study 1 **Research Highlights**
Research conducted with 126 patients with chronic diseases, revealed that Maharishi Ayurvedic treatment (consisting of diet, herbal formulas, and daily routines) was able to bring about a substantial improvement in seven of ten chronic diseases, even in cases where the disease had existed for many years.

Research on Physiological Effects

1. **Title**

Effect of the Herbal Mixture MAK-4 on Organ Functions in Watanabe Heritable Hyperlipidemic (WHHL) Rabbits

Publication

Biochemical Archives, Vol. 13, pp. 285-296, 1997.

Authors

Jae Y. Lee, John A. Lott, Ellen M. Kauffman, and Hari M. Sharma.

Conducted at

Department of Pathology, College of Medicine, The Ohio State University, Columbus, OH 43210

Summary

This study assessed the organ-protective effects of MAK-4 which was fed to Watanabe Heritable Hyperlipidemic (WHHL) rabbits. The control group (n = 5) was fed normal rabbit chow and the experimental group (n = 6) was fed 6% (w/w) MAK-4-supplemented chow, for 6 months. Blood specimens were drawn from the ear vein at the start of the experiment before MAK-4 was given, and after 2, 4, and 6 months of MAK-4 ingestion. Twenty-four-hour urines were collected between the 25th and 26th week. Various biochemical parameters were assessed, including tests for liver function, kidney function, pancreatic function, enzymes, and other tests for tissue damage. Results showed that albumin, fibrinogen, and total protein were significantly higher ($p < 0.05$) in the MAK-4 group compared to the control group. Gamma glutamyl transferase, creatine kinase, creatine kinase-MM isoenzyme, and lipid peroxide were significantly decreased in the MAK-4-treated group as compared to the controls. Creatinine, urine inorganic phosphorus, urine uric acid, urine amylase, and urine glucose were significantly lower ($p < 0.05$) in the MAK-4 group compared to the control group. Glutathione peroxidase activity, mean corpuscular hemoglobin concentration, and superoxide dismutase were significantly increased ($p < 0.05$) in the MAK-4 group compared to the controls. These findings suggest prevention of organ damage in the MAK-

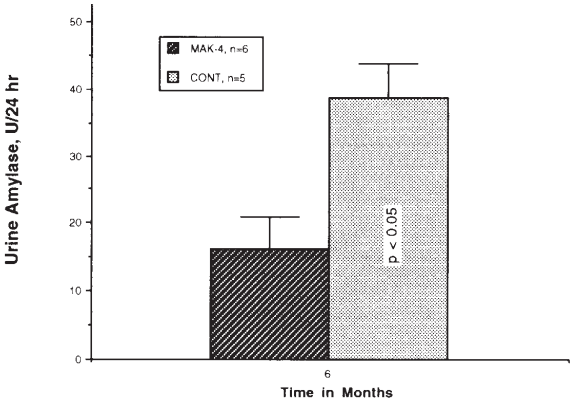


Figure 2: Effect of 6% MAK-4 supplemented diet on urine amylase in Watanabe Heritable Hyperlipidemic rabbits after 6 months. CONT: control group. Values are mean ± SE.

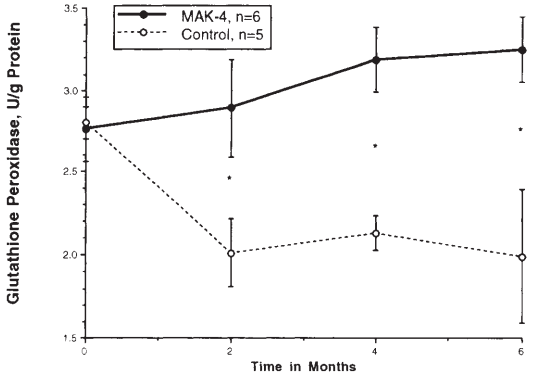


Figure 3: Effect of 6% MAK-4 supplemented diet on glutathione peroxidase in Watanabe Heritable Hyperlipidemic rabbits during a 6 month study period. Values are mean ± SE. *p<0.05.

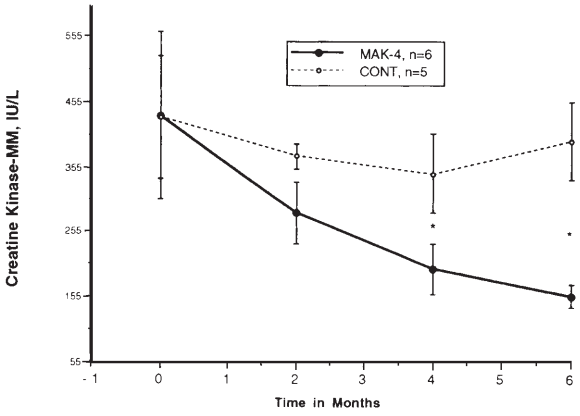


Figure 4: Effect of 6% MAK-4 supplemented diet on creatine kinase in Watanabe Heritable Hyperlipidemic rabbits during a 6 month study period. CONT: control group. Values are mean ± SE. p<0.05.

4-supplemented rabbits. The mechanism of action may be prevention of lipid and protein oxidation by MAK-4.

Study 1 **Research Highlights**
Wanatabe Heritable Hyperlipidemic rabbits fed MAK-4 for 6 months showed significantly increased glutathione peroxidase activity, mean corpuscular hemoglobin concentration and superoxide dismutase, as compared with the control group. These findings suggest prevention of organ damage in the MAK-4 supplemented rabbits, which may be due to prevention of lipid and protein oxidation by MAK-4.

2. Title

Subjective Survey, Blood Chemistry and Complete Blood Profile of Subjects Taking Maharishi Amrit Kalash (MAK)

Publication

Federation of the American Societies for Experimental Biology Journal, Vol. 5, No. 5, p. A1317, 1991 (Abstract).

Authors

K.S. Blasdell,* H.M. Sharma,** P.F. Tomlinson, Jr.,* and R.K. Wallace.*

Conducted at

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**Ohio State University, Columbus, OH 43210

Summary

Psychophysiological changes are reported in subjects regularly taking MAK (MAPI, Inc., Lancaster, MA), an herbal food supplement demonstrating antineoplastic, antioxidant and anti-aging activities in animal and in in-vitro studies. Six hundred fifty-nine subjects (age 41±9, taking MAK 22±11 mos) reported substantial benefits in 19 psychophysiological indices, e.g., increased resistance to illness 87%; happiness 84%; energy 78%; tranquility 83%; mental clarity and emotional balance 80%. Remaining subjects noted no change or condition worsened, ≤ 1%. A substantial percentage of previous sufferers (46 on medical treatment) reported benefits on 21 illnesses, e.g. colds 94% improved or eliminated, n=209; PMS 84%, 120; constipation 87%, 245; hay fever 81%, 118; headaches 78%, 148; fatigue 88%, 249; asthma 82%, 28; cancer 90%, 10; rheumatoid arthritis 73%, 22; autoimmunity 100%, 10. Only 3% (n=22) reported minor complaints, e.g. bad taste; sugar rush; upset stomach; and diarrhea. Blood chemistry (24 values) and complete blood profile in 82 separate volunteers showed no abnormal findings associated with MAK intake. Substantial benefits indicate that MAK may be valuable as a preventive agent, a therapeutic adjunct and a safe candidate for clinical trials.

Study 2 **Research Highlights**
Data from 659 human subjects showed that regularly taking MAK carried substantial benefits in 19 psychophysiological indices and on 21 illnesses, with no abnormal effects, as evaluated by blood chemistry and complete blood profiles. Therefore, MAK may be valuable as a preventive agent, a therapeutic adjunct and a safe candidate for clinical trials.

Research on Primordial Sound

1. **Title**
Effect of Different Sounds on Growth of Human Cancer Cell Lines In Vitro

Publication
Alternative Therapies in Clinical Practice, Vol. 3, No. 4, pp. 25-32, 1996.

Authors
Hari M. Sharma, MD, FRCPC, Ellen M. Kauffman, MT, HTL (ASCP), and Ralph E. Stephens, PhD.

Conducted at
Department of Pathology, College of Medicine, The Ohio State University, Columbus, OH

Summary
Sound has an effect on plants and on the human physiology. Cells vibrate dynamically and may transmit information via harmonic wave motions. This study compared the effects of "primordial sounds" (Sama Veda, from the Maharishi Ayur-Veda system of natural health care), or hard rock music (AC/DC, "Back in Black"), and no sound on the growth of cells in culture. Five human tumor cell lines (lung, colon, brain, breast, and skin) and one normal cell line (fibroblasts) were tested in triplicate for each of an average of four experiments. The recordings of Sama Veda and "Back in Black" were normalized to maintain the same maximum amplitudes, with no significant effect on the results. Primordial sound significantly decreased the average growth across cell lines (p=0.005, ANOVA). In the presence of hard rock music, growth of cells was significantly increased (p=0.03), but the effect was not consistent. We conclude that sound has an effect on the growth of neoplastic and normal human cells in vitro.

Table 1. Sound-induced changes in cell growth

Tissue/organ	Classification	Cell line	percent change
No sound vs. Primordial sound			
Brain	Malignant glioma	U251-MG	- 25.3
Breast	Adenocarcinoma	MCF7	- 16.9
Colon	Adenocarcinoma	HT29	- 19.9
Lung	Carcinoma	A549	- 22.4
Skin	Malignant melanoma	RPMI7951	- 12.4
Skin	Normal fibroblasts	NHDF	- 13.9
No sound vs. Hard rock music			
Tissue/organ	**Classification**	**Cell line**	**percent change**
Brain	Malignant glioma	U251-MG	+ 22.1
Breast	Adenocarcinoma	MCF7	+ 26.9
Colon	Adenocarcinoma	HT29	+ 14.1
Lung	Carcinoma	A549	+ 6.1
Skin	Malignant melanoma	RPMI 7951	(Only one experiment)
Skin	Normal fibroblasts	NHDF	+ 10.2

Primordial sound (Sama Veda) decreased average growth across cell lines (p = 0.005, ANOVA) as compared to no music, after controlling in our statistical model for cell line and day of experiment. In the presence of hard rock music (AC/DC, "Back in Black") growth of cells was increased (p = 0.03, ANOVA) compared to no music after controlling for cell line and day of experiment, but the effect was not consistent.

Study 1 **Research Highlights**
In the presence of primordial sounds, average growth across five human tumor cell lines and one normal cell line (fibroblasts) decreased. In the presence of hard rock music, growth of tumor cells significantly increased, but the effect was not consistent. Thus, sound has an effect on the growth of neoplastic and normal human cells in vitro.

Research on the Maharishi Rejuvenation[SM] Program

1. **Title**

Improvement in Cardiovascular Risk Factors Through Panchakarma[§] Purification Procedures

Publication

The Journal of Research and Education in Indian Medicine, Vol. 12, No. 4, pp. 3-13, 1993.

Authors

Hari M. Sharma,* Sanford I. Nidich,** David Sands,† and D. Edwards Smith.†

Conducted at

* Department of Pathology, College of Medicine, The Ohio State University, Columbus, OH

**Department of Science of Creative Intelligence and †Laboratory for Preventive Medicine, Department of Physiological and Biological Sciences, Maharishi International University, Fairfield, IA

Summary

Maharishi Ayur-Veda uses Maharishi Panchakarma[§] (PK) for eliminating impurities, purifying and balancing the physiology, and clearing the channels. PK consists of oleation (use of clarified butter), virechana (purgation), abhyanga (medicated whole-body massage), shirodhara (flow of medicated oil on forehead), swedena (herbalized fomentation), nasya (nasal administration of herbs), and basti (herbalized enemas). PK was given for 3-5 days to 31 subjects (15 male and 16 female), with a mean age of 40.6 years. Fasting blood samples were tested for biochemical parameters before (visits A and B), during (visit C), 1 week following (visit D), and 2.9 months following (visit E) PK. Vasoactive intestinal peptide (VIP), a coronary vasodilator, rose a significant 80% by 2.9 months after PK. Total cholesterol fell acutely in all subjects and HDL cholesterol rose 7.5% (p=0.015) after 2.9 months if original values were <15 mg/dL. Lipid peroxide, a measure of free radical damage, rose during PK, then fell to lower levels at 2.9 months. Pulse and diastolic blood pressure were reduced after PK. State anxiety measures improved significantly. These results indicate that PK is useful in improving cardiovascular risk factors.

Vasoactive Intestinal Peptide : The initial value of **VIP** (n=31) was pg/mL in all but 5 subjects. It remained essentially unchanged at visits A through D but then rose a dramatic 80% from A to E, p=0.003, and 84% from B to E, p=0.004, using a paired, two-tailed t-test **(Figure.1)**.

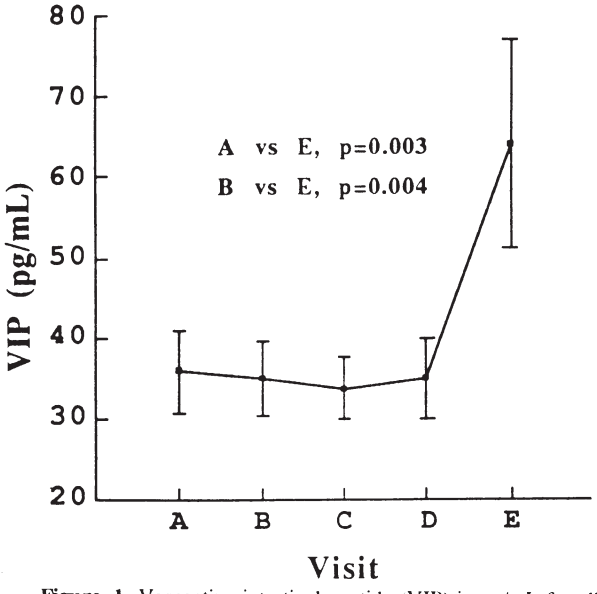

Figure. 1 Vasoactive intestinal peptide (VIP) in pg/mL for all subjects Means and Standard Error of the Mean (SEM) for each visit.

[§] Maharishi Panchakarma is another name for the Maharishi Rejuvenation[SM] Program

(continued)

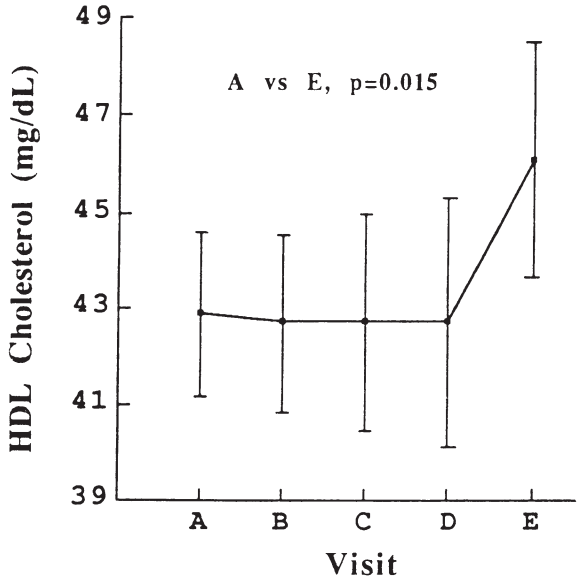

Figure. 3 HDL cholesterol in mg/dL for those subjects (n=13) whose initial values at A were <50 mg/dL. Means and SEM for visit.

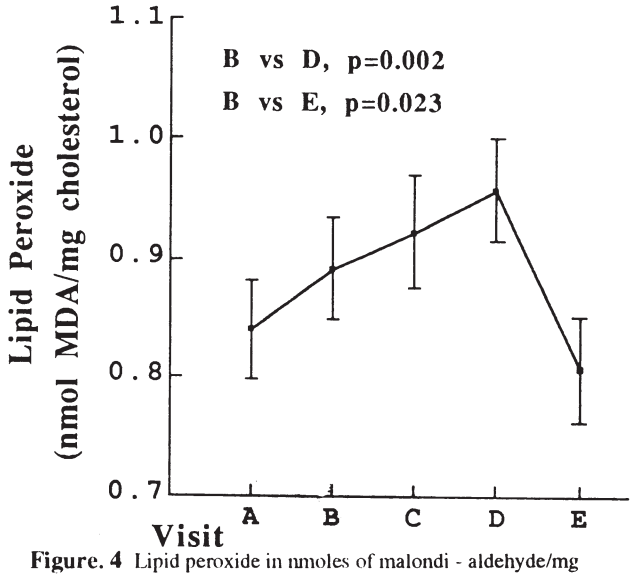

Figure. 4 Lipid peroxide in nmoles of malondi - aldehyde/mg cholesterol for all subjects (n=27). Means and SEM for each visit.

Table 2 : Means, Standard Deviations, and Change Score on State Anxiety for **PK** and Control Groups.

GROUP		PRE TEST (VISIT A)		POST TEST (VISIT B)		ADJUSTED CHANGE
	N	M	SD	M	SD	M
PK	27	29.778	7.827	26.111	7.013	-3.934*
Control	28	30.750	8.847	31.679	8.857	+1.186

M=mean , N= sample size, SD = standard deviation. *$p < 0.025$

Study 1 **Research Highlights**
Maharishi Panchakarma (PK) administered to human subjects for 3 to 5 days showed usefulness in improving cardiovascular risk factors.

2. Title
Influence of Maharishi Ayur-Veda Purification Treatment on Physiological and Psychological Health

Publication
Erfahrungsheilkunde—Acta Medica Empirica (German medical journal), Vol. 11, pp. 720-729, 1988.

Author
Rainer Waldschutz.

Conducted at
Albert-Ludwigs University, Freiburg, Germany

Summary

Maharishi Panchakarma[§], one of the many aspects of Maharishi Ayur-Veda, aims at purifying and balancing the physiology. This therapy includes herbalized oil massage (abhyanga), herbalized steam treatment (swedana), pouring of herbalized oil on the forehead (shirodhara), medicated enemas (basti), laxative treatment (virechana), and other forms of treatment. This study was conducted to assess the effects of Maharishi Panchakarma in the areas of physiology and psychology. Total cholesterol, triglycerides, creatinine, urea, uric acid, and glucose were measured before and immediately after a two-week treatment period on up to 93 patients. Psychological evaluation was made using the Freiburger Personality Inventory (FPI), which was administered to 106 subjects before, immediately after, and 6-8 weeks after treatment. Results showed reductions in total cholesterol from 203.5 mg/dL to 179.5 mg/dL ($n=82$, $p<0.001$), and in urea from 23.9 mg/dL to 20.4 mg/dL ($n=70$, $p<0.01$). Uric acid, triglycerides, creatinine, and glucose did not show significant changes. Over the two-week treatment period, significant changes on 6 of the 12 FPI scales were observed, including reductions in bodily complaints, irritability, bodily strain, psychological inhibition, and openness, as well as greater emotional stability. Psychological testing six to eight weeks after treatment showed evidence of sustained benefits for mental health and well-being. No significant changes were observed in physiological or psychological parameters in 10 control subjects, except for a temporary increase in aggression. These findings support the results of previous research on Maharishi Panchakarma indicating its effectiveness in improving physiological and psychological health.

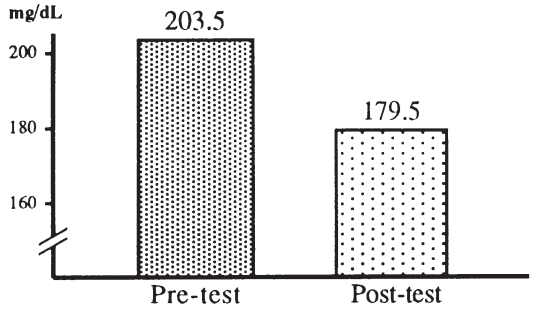

Figure 1: Change in Total Cholesterol

Total cholesterol was measured in 82 subjects at the time of Pre- and Post-test. The average change was 10.5% (203.5 mg/dL at Pre-test and 179.5 mg/dL at Post-test).

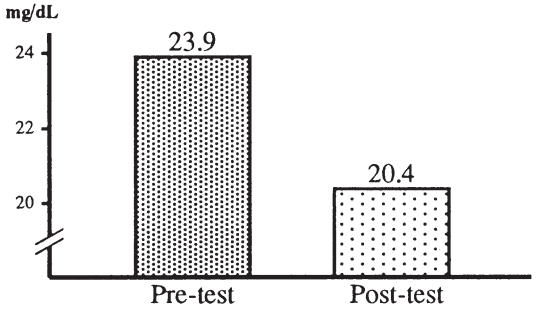

Figure 2: Change in Urea

Urea was measured in 70 subjects at the time of Pre- and Post-test. The average change was 11% (23.9 mg/dL at Pre-test and 20.4 mg/dL at Post-test).

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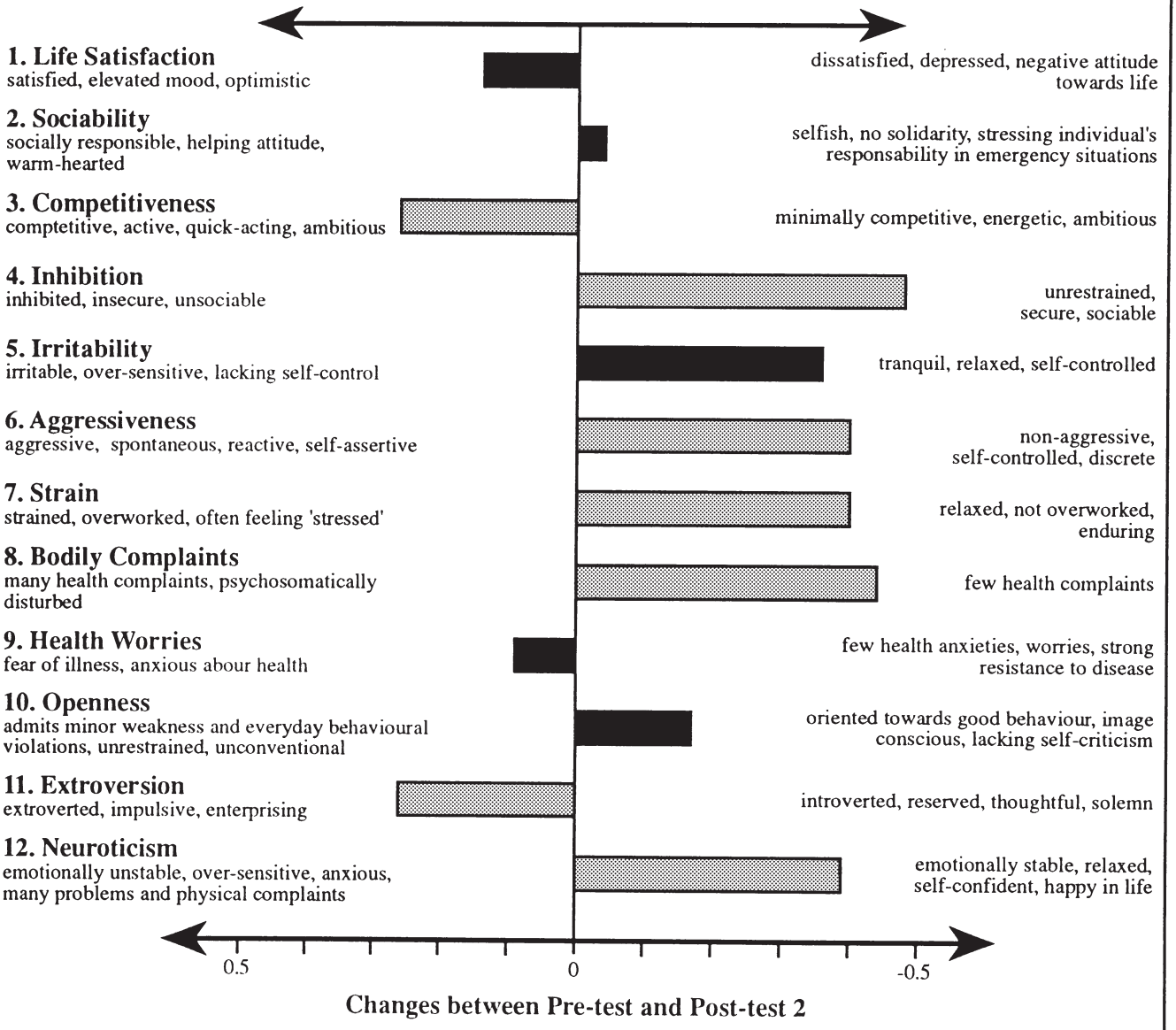
Figure 3: Psychological Changes as Measured by the Freiburger Personality Inventory



The Freiburger Personality Inventory was used in 106 experimental subjects at Pre-test, Post-test 1 and Post-test 2. The changes between Pre-test and Post-test 2 are shown above. Significant changes are shown in bright color and non-significant changes in dark color.

Study 2 **Research Highlights**
The findings of this study, conducted with human subjects, support the results of previous research on Maharishi Panchakarma, indicating its effectiveness in improving physiological and psychological health.

3. Title

Health Promotion With a Traditional System of Natural Health Care: Maharishi Ayur-Veda

Publication

Journal of Social Behavior and Personality, Vol. 5, No. 3, pp. 1-27, 1990.

Authors

Robert H. Schneider,* Kenneth L. Cavanaugh,** H.S. Kasture,† Stuart Rothenberg,†† Richard Averbach,†† Donald Robinson,* and Robert Keith Wallace.*

Conducted at

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††Institute for Ayurvedic Studies, Maharishi International University, Fairfield, IA 52556

Summary

This study investigated the Maharishi Ayur-Veda Panchakarma[§] program and its effects on self-reported mental and physical health. This program includes a set of physiological therapies that are recommended on a periodic basis for enhancement of physiological homeostasis and promotion of mental and physical health. In a first pilot study, 142 subjects were surveyed after a 1-2 week Maharishi Ayur-Veda Panchakarma program for changes in health symptoms compared to 60 control subjects who participated in a didactic class for the same period of time. In the second follow-up study, 62 consecutive subjects were tested before and after a similar Maharishi Ayur-Veda Panchakarma program with the Profile of Mood States (POMS) and compared to 71 controls participating in a didactic class. The results for the pilot study showed that the experimental subjects reported significantly greater improvements in well-being, energy-vitality, strength-stamina, appetite and digestive patterns, previous complaints generally, and rejuvenation and youthfulness than control subjects ($p=0.05$ to <0.00001). Sleep patterns changed nonsignificantly. In the second study, the experimental subjects decreased significantly more than controls on overall distress ($p=0.003$). On the POMS subscales, anxiety, depression, and fatigue decreased, and vigor increased significantly more for the experimental group than the controls ($p=0.03$ to 0.003). Confusion decreased marginally ($p=0.06$) and anger decreased nonsignificantly. These preliminary findings suggest that the Maharishi Ayur-Veda Panchakarma program is associated with improvements in mental and physical health symptoms, at least in selected subjects. This traditional program of natural health care may help to address current public health demands for efficacious and practical health-promotion and disease-prevention programs.

[§] Maharishi Panchakarma is another name for the Maharishi Rejuvenation[SM] Program

Study 3 **Research Highlights**

Preliminary research shows that the Maharishi Ayurveda Panchakarma program is associated with improvements in mental and physical health symptoms, at least in selected human subjects. Thus, this program may help to address current public health demands for efficacious and practical health-promotion and disease-prevention programs.

4. Title

Selective Growth Inhibition of a Human Malignant Melanoma Cell Line by Sesame Oil In Vitro

Publication

Prostaglandins, Leukotrienes and Essential Fatty Acids, Vol. 46, pp. 145-150, 1992.

Authors

D. Edwards Smith and J.W. Salerno.

Conducted at

Laboratory for Preventive Medicine, Department of Physiological and Biological Sciences, Maharishi International University, Fairfield, IA 52556

Summary

Ayurveda, an ancient and comprehensive system of natural medicine, recommends regular topical application to the skin of sesame oil, above all other oils, as a health-promoting procedure. We examined the effect of sesame oil and several other vegetable oils and their major component fatty acids on the proliferation rate of human normal and malignant melanocytes growing at similar rates in serum-free media. We found that sesame and safflower oils, both of which contain large amounts of linoleate in triglyceride form, selectively inhibited malignant melanoma growth over normal melanocytes, whereas coconut, olive, and mineral oils, which contain little or no linoleate as triglyceride, did not. These oils were tested at a range of 10-300 microgram/mL. We found that of the fatty acids tested, only linoleic acid was selectively inhibitory, while palmitic and oleic were not. These fatty acids were tested in the range of 3-100 microgram/mL. These results suggest that certain vegetable oils rich in linoleic acid, such as sesame oil recommended for topical use by Ayurveda, may contain selective antineoplastic properties which are similar to those demonstrated for essential polyunsaturated fatty acids and their metabolites. This suggests that whole vegetable oils may have potential clinical usefulness.

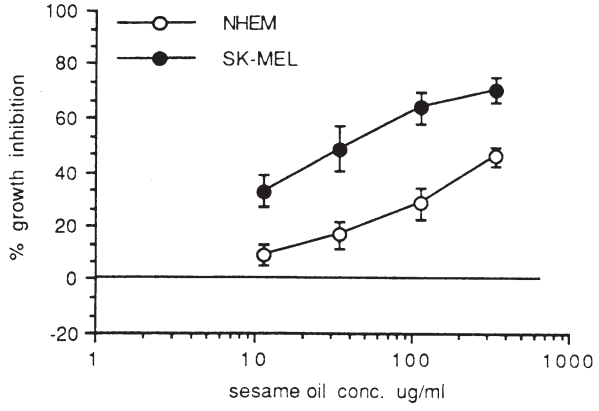

Fig. 2 Growth inhibiting effect of whole undigested sesame oil on the (SK-MEL ●) human malignant melanoma and (NHEM ○) normal human epidermal melanocytes. Dosage range was 10, 30, 100 and 300 μg/ml plotted on logarithmic scale. All cells seeded at 1×10^4 per cm^2 (or 4×10^4 per well) in 12-well TC plates. Each well contained 2 ml MGM (melanocyte growth medium — no serum). Sesame oil added on day 2 and all cells harvested and counted together on day 5. Average growth (fold increase) over 5 days was 2.6 for NHEM and 2.2 for SK-MEL. Each point represents the mean and SEM of 12 experiments. $F(1, 11) = 13$, $p = 0.004$

Study 4 **Research Highlights**

In vitro research results suggest that certain vegetable oils rich in linoleic acid, such as sesame oil recommended for topical use in Ayurveda, may contain selective antineoplastic properties that are similar to those demonstrated for essential polyunsaturated fatty acids and their metabolites.

5. Title

The Use of Sesame Oil and Other Vegetable Oils in the Inhibition of Human Colon Cancer Growth In Vitro

Publication

Anticancer Research, Vol. 11, pp. 209-216, 1991.

Authors

John W. Salerno and D. Edwards Smith.

Conducted at

Department of Physiological and Biological Sciences, Maharishi International University, Fairfield, IA 52556

Summary

Sesame contains large quantities of the essential polyunsaturated fatty acid (PUFA), linoleic acid, in the form of triglycerides. The antineoplastic properties of many PUFAs such as linoleic acid and their metabolites are known. This study tested the hypothesis that natural vegetable oils, such as sesame oil and its component linoleic acid, when added to human colon adenocarcinoma cells growing in tissue culture, would inhibit their growth and that normal colon cells would not be similarly affected. Three human colon cancer cell lines and one normal human colon cell line were exposed to the following: (1) pure linoleic acid; (2) lipase-digested sesame oil; (3) undigested sesame oil; (4) five additional common vegetable oils; (5) mineral oil. Linoleic acid inhibited the in vitro growth of all three malignant human colon adenocarcinoma cell lines. The normal colon cell line showed dramatically less inhibition of growth. Lipase-digested sesame oil (LDSO) and undigested sesame oil (UDSO) produced greater inhibition of growth of all three malignant colon cell lines than of the normal colon cells. Five other common vegetable oils containing various amounts of PUFAs, such as corn, soybean, safflower, olive, and coconut oils, all in their lipase-digested form, were found to dramatically inhibit the growth of the HT-29 malignant human colon cell line. Undigested olive and safflower oils also inhibited the HT-29 cells, although not as markedly as the lipase-digested oils. Mineral oil did not inhibit the growth of HT-29 cells. Both lauric and palmitic acid, which are saturated fatty acids found in abundance in coconut oil, inhibited the HT-29 cells more strongly than linoleic acid, while oleic acid did not inhibit. These results indicate that many vegetable oils, including sesame, contain in vitro antineoplastic properties; this finding warrants further investigation both in vitro and in vivo to assess their possible chemotherapeutic potential.

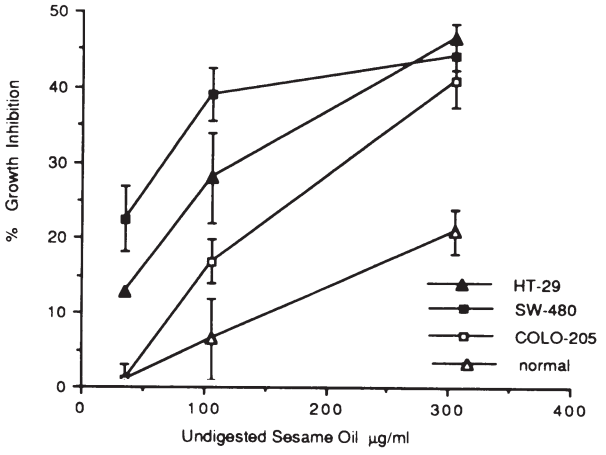

Figure 3. *Growth inhibiting effect of whole undigested sesame oil at doses of 30, 100, 300 µg/ml on the growth rate of three human colon adenocarcinoma and one normal human colon cell line. Each point represents the mean and SEM of four experiments.*

Study 5 **Research Highlights**

In vitro research with human colon cancer cell lines indicates that many natural vegetable oils, including sesame, contain in vitro antineoplastic properties. Further in vivo and in vitro investigation is warranted in order to assess oils' possible chemotherapeutic potential.

Research on the Transcendental Meditation® Program

1. Title

A Randomized Controlled Trial of Stress Reduction for Hypertension in Older African Americans

Publication

Hypertension, Vol. 26, pp. 820-827, 1995.

Authors

Robert H. Schneider,* Frank Staggers,** Charles N. Alexander,† William Sheppard,** Maxwell Rainforth,† Kofi Kondwani,† Sandra Smith,** and Carolyn Gaylord King.†

Conducted at

* Center for Health and Aging Studies, Department of Physiological and Biological Sciences, Maharishi University of Management, Fairfield, IA

**The Hypertension and Stress Management Research Clinic, West Oakland Health Center, Oakland, CA

† Department of Psychology, Maharishi University of Management, Fairfield, IA

Summary

This study investigated the short-term efficacy and feasibility of two stress education approaches to the treatment of mild hypertension in older African Americans. This was a randomized, controlled, single-blind trial with 3 months of follow-up in a primary care, inner-city health center. Of 213 African American men and women screened, 127 individuals (aged 55 to 85 years with initial diastolic pressure of 90 to 109 mm Hg, systolic pressure of $\leq$189 mm Hg, and final baseline blood pressure of $\leq$179/104 mm Hg) were selected. Of these, 16 did not complete follow-up blood pressure measurements. Mental and physical stress-reduction approaches (Transcendental Meditation and progressive muscle relaxation) were compared with a lifestyle modification education control program and with each other. The primary outcome measures were changes in clinic diastolic and systolic pressures from baseline to final follow-up, measured by blinded observers. The secondary measures were linear blood pressure trends, changes in home blood pressure, and intervention compliance. Adjusted for significant baseline differences and compared with control, Transcendental Meditation reduced systolic pressure by 10.7 mm Hg ($p<0.0003$) and diastolic pressure by 6.4 mm Hg ($p<0.00005$). Progressive muscle relaxation lowered systolic pressure by 4.7 mm Hg ($p=0.054$) and diastolic pressure by 3.3 mm Hg ($p<0.02$). The reductions in the Transcendental Meditation group were significantly greater than in the progressive muscle relaxation group for both systolic blood pressure ($p=0.02$) and diastolic blood pressure ($p=0.03$). Linear trend analysis confirmed these patterns. Compliance was high in both stress-reduction groups. Home systolic but not diastolic pressure changes were similar to clinic changes. Selected mental and physical stress-reduction techniques demonstrated efficacy in reducing mild hypertension in this sample of older African Americans. Of the two techniques, Transcendental Meditation was approximate-

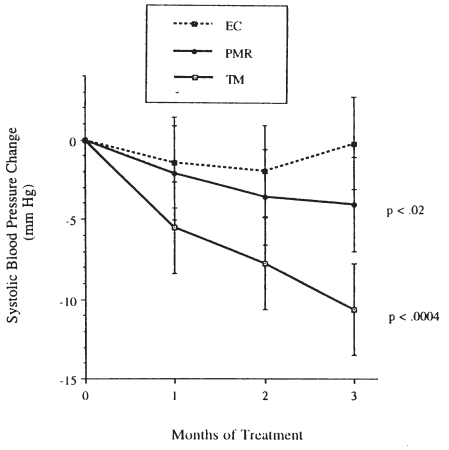

FIG 1. Line graph shows mean changes in clinic systolic pressure over 3 months (follow-up minus baseline) with SEM. Probability values are for repeated-measures ANCOVA comparing each experimental group (TM and PMR) with control (EC). TM indicates Transcendental Meditation (n=36); PMR, progressive muscle relaxation (n=33); and EC, lifestyle modification education control (n=35).

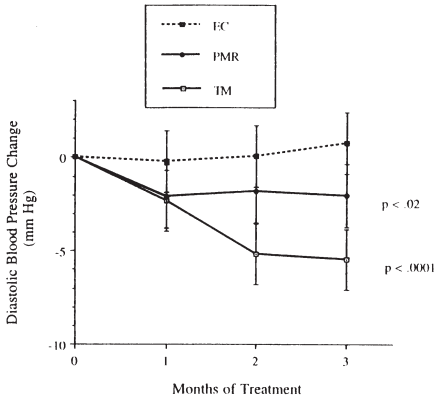

FIG 2. Line graph shows mean changes in clinic diastolic pressure over 3 months (follow-up minus baseline) with SEM. Probability values are for repeated-measures ANCOVA comparing each experimental group (TM and PMR) with control (EC). TM indicates Transcendental Meditation (n=36); PMR, progressive muscle relaxation (n=33); and EC, lifestyle modification education control (n=35).

ly twice as effective as progressive muscle relaxation. Long-term effects and generalizability to other populations require further evaluation.

Study 1 **Research Highlights**
The effects of Transcendental Meditation and progressive muscle relaxation were compared in African-American men and women with elevated blood pressure. Of the two techniques, Transcendental Meditation was approximately twice as effective as progressive muscle relaxation in reducing both systolic and diastolic blood pressure.

2. Title
Cost-Effective Hypertension Management: Comparison of Drug Therapies With an Alternative Program

Publication
The American Journal of Managed Care, Vol. 2, pp. 427-437, 1996.

Authors
Robert E. Herron, PhD,* Robert H. Schneider, MD,** Joseph V. Mandarino, PhD,† Charles N. Alexander, PhD,** and Kenneth G. Walton, PhD.††

Conducted at
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**Center for Health and Aging Studies, Department of Physiological and Biological Sciences, and
† Department of Management, and
††Departments of Chemistry and Physiology, Maharishi University of Management, Fairfield, IA

Summary
The competitive nature of managed care organizations demands that providers seek cost-effective ways to maintain the health of their clients. As an approach to reducing cardiovascular morbidity and mortality, antihypertensive medication is costly, has adverse side effects, and has questionable value in reducing coronary heart disease. This report evaluates a behavioral stress-reduction method as an option to pharmaceutical treatment. Randomized studies indicate that the Transcendental Meditation® (TM) technique reduces mild hypertension (the predominant form of hypertension) as effectively as do drug therapies. A cost-effectiveness comparison in 1996 dollars was conducted among five standard antihypertensive medications and the TM technique over a simulated 20-year treatment period. According to present value analysis of treatment payments, the TM technique had the lowest present value cost, and thus appeared to be the most attractive alternative. The estimated average cost of antihypertensive drug treatment ranged from $375 per year for hydrochlorothiazide to $1,051 per year for propranolol hydrochloride, whereas the estimated average cost of treatment with the TM technique was $286 per year. When combined with results of controlled trials documenting the effectiveness of the TM technique in reducing high blood pressure, decreasing morbidity and mortality, and improving the quality of life, the present comparison suggests that this nonpharmacologic procedure may be safely used as a cost-effective treatment of hypertension in the managed care setting.

Study 2 **Research Highlights**
In a cost-effectiveness comparison, the estimated average cost of antihypertensive drug treatment ranged from $375 per year for hydrochlorothiazide to $1,051 per year for propranolol hydrochloride, whereas the estimated average cost of treatment with the Transcendental Meditation technique was $286 per year.

3. Title

Usefulness of the Transcendental Meditation Program in the Treatment of Patients With Coronary Artery Disease

Publication

The American Journal of Cardiology, Vol. 77, pp. 867-870, 1996.

Authors

John W. Zamarra, MD, Robert H. Schneider, MD, Italo Besseghini, MD, Donald K. Robinson, MS, and John W. Salerno, PhD.

Conducted at

The Department of Medicine, State University of New York, Buffalo, NY; Veterans Administration Hospital, Buffalo, NY; and the Center for Health and Aging Studies, Maharishi University of Management, Fairfield, IA

Summary

This investigation was designed as a pilot study to test the hypothesis that stress reduction intervention with the Transcendental Meditation (TM) program would reduce exercise-induced myocardial ischemia in patients with known coronary artery disease. Twenty-one patients with documented coronary artery disease were prospectively studied. After baseline symptom-limited exercise tolerance testing, subjects were assigned to practice the TM technique or allocated to a wait-list control group. Single blind testing was repeated after an average 7.6 months of follow-up. Results showed that the patients who learned TM demonstrated significantly greater exercise tolerance, higher maximal workload, delayed onset of ST-segment depression, and decreases in double product at each exercise interval, compared with the control group. The reliability of the test data for assessing changes in exercise performance was supported by the relatively high reproducibility of the symptom-limited exercise tolerance test measures at baseline. The results suggest that practice of the Transcendental Meditation program is useful in reducing exercise-induced myocardial ischemia in patients with coronary artery disease and may be considered beneficial for the prevention and treatment of coronary artery disease.

Study 3 **Research Highlights**

Human study results suggest that the Transcendental Meditation program is useful in reducing exercise-induced myocardial ischemia in patients with coronary artery disease and may be considered beneficial for the prevention and treatment of coronary artery disease.

4. Title

The Impact of the Transcendental Meditation Program on Government Payments to Physicians in Quebec: An Update

Publication

American Journal of Health Promotion, Vol. 14, No. 5, pp. 284-291, 2000.

Authors

Robert E. Herron* and Stephen L. Hillis**

Conducted at

* Department of Management and Public Administration, Maharishi University of Management, Fairfield, IA 52557

** Department of Statistics and Actuarial Science, University of Iowa, Iowa City, IA

Summary

This study expands upon a previous study conducted by the authors to analyze whether practice of the Transcendental Meditation (TM) technique affected government payments to physicians in Quebec, Canada. The present study includes data on an additional 741 practitioners of the TM technique (for a total of 1418 TM subjects) and a comparison subject for each TM practitioner, and extends the time period three additional years. This retrospective, longitudinal study compared data on government payments to physicians for treating 1418 health insurance enrollees in Quebec who practiced TM and 1418 comparison subjects who did not practice TM. Data for pre-intervention and post-intervention periods over a time period of 14 years was analyzed. The TM subjects had practiced TM for an average of 6.7 years and participated in the study by filling out a questionnaire. They were considered a convenience sample since they were self-selected, the number of questionnaires distributed was not known, and the number of possible respondents was not known. The comparison group for this study was randomly selected by the Quebec health insurance agency, matching each TM subject with a comparison subject having the same age, gender, and region in which they lived. The total number of study subjects was 2836, including 1408 men and 1428 women, with an average age of 38 years. The subjects' annual physician expenses for the years 1981-1994 were adjusted for inflation and analyzed in constant 1992 Canadian dollars. For the preintervention period (before subjects started the TM technique), the yearly rate of increase in payments to physicians was not significantly different between the TM and comparison groups. For the post-intervention period (after the subjects started TM), the yearly payments to physicians for the comparison group increased to levels that were higher than the preintervention levels for this group, increasing up to 11.73% annually over a six-year period. In the TM group however, the yearly payments decreased 1% to 2% annually in the post-intervention period, resulting in a significant mean annual difference of 13.78% ($p=0.0017$), compared to the non-TM group. These data suggest that practice of the TM technique reduced payments to physicians between 5% and 13% per year over a six-year period, compared to the control group. This type of reduction in medical expenditures could result in billions of dollars saved by governments and private health insurance companies in nations experiencing rapidly rising health care costs.

Study 4 **Research Highlights**

This retrospective, longitudinal study compared data on Canadian government payments to physicians for treating health insurance enrollees who practiced Transcendental Meditation (TM) with comparison subjects who did not practice TM. The data suggest that practice of the TM technique reduced payments to physicians between 5% and 13% per year over a six-year period, compared with the control group.

Additional research on Transcendental Meditation:

The following five volumes contain more than 500 research studies conducted on the Transcendental Meditation and TM-Sidhi techniques during the past 25 years:

1. Orme-Johnson DW, Farrow JT (eds). Scientific Research on the Transcendental Meditation Program: Collected Papers, Volume 1. Rheinweiler, Germany: MERU Press, 1977.

2. Chalmers RA, Clements G, Schenkluhn H, Weinless M (eds). Scientific Research on Maharishi's Transcendental Meditation and TM-Sidhi Program: Collected Papers, Volume 2. Vlodrop, The Netherlands: MVU Press, 1989.

3. Chalmers RA, Clements G, Schenkluhn H, Weinless M (eds). Scientific Research on Maharishi's Transcendental Meditation and TM-Sidhi Program: Collected Papers, Volume 3. Vlodrop, The Netherlands: MVU Press, 1989.

4. Chalmers RA, Clements G, Schenkluhn H, Weinless M (eds). Scientific Research on Maharishi's Transcendental Meditation and TM-Sidhi Program: Collected Papers, Volume 4. Vlodrop, The Netherlands: MVU Press, 1989.

5. Wallace RK, Orme-Johnson DW, Dillbeck MC (eds). Scientific Research on Maharishi's Transcendental Meditation and TM-Sidhi Program: Collected Papers, Volume 5. Fairfield, IA: MIU Press, 1989.

Note: The most recent research on Transcendental Meditation can be viewed at www.tm.org.

Bibliography

1. Sharma, H. and Clark, C. ***Contemporary Ayurveda: Medicine and Research in Maharishi Ayur-Veda.*** London: Churchill Livingstone, 1998.

2. Sharma, H. ***Awakening Nature's Healing Intelligence: Expanding Ayurveda Through the Maharishi Vedic Approach to Health.*** Twin Lakes, WI: Lotus Press, 1997.

3. Sharma, H. ***Freedom from Disease: How to Control Free Radicals, a Major Cause of Aging and Disease.*** Toronto: Veda Publishing, 1993.

4. Lonsdorf, N., Butler, V., and Brown, M. ***A Woman's Best Medicine: Health, Happiness, and Long Life Through Maharishi Ayurveda.*** New York: Jeremy P. Tarcher/Putnam, 1993.

5. Wallace, R. K. ***The Physiology of Consciousness.*** Fairfield, IA: MIU Press, 1993.

Ingredients of Herbal Mixtures

1. **Maharishi Amrit Kalash**

   MAK-4 Herbal Fruit Concentrate (Also known as **M-4** or **Maharishi Amrit Kalash Nectar**):
   Indian Gooseberry, Indian Gallnut, Cardamom, Cinnamon, Long Pepper (Catkins), Indian Pennywort, Cyperus, Nutgrass, White Sandalwood, Aloeweed, Butterfly Pea, Ceylon Ironwood, Turmeric, Ghee (Clarified Butter—acts as a carrier to help assimilation), Whole Cane Sugar, Honey. Processed in the extracts of: Bengal Quince, Indian Trumpet Flower, Cashmere Bark, Castor Oil Root, Country Mallow, Thatch Grass, Eragrostis cynosuroides, Sugar Cane, Indian Asparagus, Spreading Hogweed, Giant Potato, Indian Kudju, Trumpet Flower, Desmodium gangeticum, Uraria picta, Yellow-berried Nightshade, Indian Nightshade, Small Caltrops, Large Caltrops, Phaseolus trilobus, Teramnus labialis, Clerodendrum phlomidis, Leptadenia reticulata, Gymnema auraniticum.

   MAK-5 Herbal Tablets (Also known as **M-5** or **Maharishi Amrit Kalash Ambrosia**):
   Winter Cherry, Licorice, Giant Potato, White Musale, Indian Gooseberry, Heart-leaved Moonseed, Indian Asparagus, Indian Wild Pepper, Aloeweed, Elephant Creeper, Black Musale, Caper Plant, Indian Gum-Arabic Tree.

   A chemical analysis of these formulas indicates that they contain the following phytochemicals:
   - Polyphenols
   - Tannic acid
   - Catechin
   - Beta-carotenoids
   - Riboflavin
   - Bioflavonoids
   - Resveratrol
   - Alpha-tocopherol
   - Ascorbate
   - A large number of low-molecular-weight substances

   A review of the literature verifies that a large number of studies have been done on these phytochemicals. They have displayed a variety of beneficial effects.

References:

Hari M. Sharma, Chandradhar Dwivedi, Bryan C. Satter, Krishnamurthy P. Gudehithlu, Hussein Abou-Issa, William Malarkey, and Gopi A. Tejwani. Antineoplastic properties of Maharishi-4 [MAK-4] against DMBA-induced mammary tumors in rats. ***Pharmacology Biochemistry and Behavior,*** Vol. 35, No. 4, pp. 767-773, 1990.

Richard W. Hemingway and Peter E. Laks, editors. Plant Polyphenols: Synthesis, Properties, Significance. New York: Plenum Press, 1992.

Hari M. Sharma, Silva Hanissian, Anil K. Rattan, Stephen L. Stern, and Gopi A. Tejwani. Effect of Maharishi Amrit Kalash on brain opioid receptors and neuropeptides. Journal of Research and Education in Indian Medicine, Vol. 10, No. 1, pp. 1-8, 1991.

Paolo Scartezzini and Ester Speroni. Review on some plants of Indian traditional medicine with antioxidant activity. Journal of Ethnopharmacology, Vol. 71, pp. 23-43, 2000.

Hari M. Sharma. Free radicals and natural antioxidants in health and disease. Journal of Applied Nutrition (in press).

2. MA-631:

Mineral Pitch, Indian Bedellium, Himalayan Silver Fir, Dry Ginger, Catkins, Picrorhiza kurroa, Galls, Black Pepper, Indian Kudju, Bamboo, Chinese Cinnamon, Cinnamon, Saffron, Cardamom. Processed in the extracts of: Indian Trumpet Flower, Cashmere Bark, Small Caltrops, Aegle marmelos, Trumpet Flower, Uraria Pitch, Tinospora cordifolia, Country Mallow, Licorice, Indian Asparagus, Winter Cherry, Indian Kudju, Raisins, Mycrostylis wallichii, Globe Thistle, Cumin Seeds, Wild Cumin, Pluchea lanceolata, Inula racemosa, Baliospermum montanum, Major Catkins, Tellycheri Bark, Nut Grass, Indian Gooseberry, Chebulic myrobalans, Beleric myrobalans.

MA-631 contains the following biologically active ingredients, many of which are antioxidants:

- Bioflavonoids
- Ascorbic acid
- Thiamin
- Niacin
- Alkaloids
- Rutin

Reference:

Atef N. Hanna, Hari M. Sharma, Ellen M. Kauffman, and Howard A. I. Newman. In vitro and in vivo inhibition of microsomal lipid peroxidation by MA-631. ***Pharmacology Biochemistry and Behavior,*** Vol. 48, No. 2, pp. 505-510, 1994.

3. MA-471:

Enicostema littorale, Phyllanthus niruri, Eugenia jambolana, Melia azadirachta, Terminalia arjuna, Aegle marmelos, Asphaltum. Processed in the extracts of: Aegle marmelos, Momordica charantia.

Reference:

Amulya R. Sircar, Ramesh C. Ahuja, Shankar M. Natu, Birendra Roy, and Hari M. Sharma. Hypoglycemic, hypolipidemic and general beneficial effects of an herbal mixture MA-471. Alternative Therapies in Clinical Practice, Vol. 3, No. 5, pp. 26-31, 1996.

4. **Student Rasayana:**
Centella asiatica, Indian Valerian, Kut Root, Indian Asparagus, Winter Cherry, Embelia ribes, Indian Sweet Fennel, Lesser Cardamom, Botea frondosakoen, Babul Tree.

The chemical composition of Student Rasayana includes the following:

- Ascorbic acid
- Thiamine
- Riboflavin
- Niacin
- Bioflavonoids
- Beta carotene
- Triterpenoids
- Sitosterol
- Centoic and Centelliac Acid
- Volatile Oil (Ethereal Valerianic Oil)
- Liquid Resin
- Essential Oil
- Glucoside
- Alkaloid Saussurine and Somniferin
- Tannin
- Inulin
- Sarsasapogenin
- Saponins
- Embelin

Reference:

Hari M. Sharma, Atef N. Hanna, Ellen M. Kauffman, and Howard A.I. Newman. Effect of herbal mixture Student Rasayana on lipoxygenase activity and lipid peroxidation. Free Radical Biology and Medicine, Vol. 18, No. 4, pp. 687-697, 1995.

5. **Maharishi Coffee Substitute** (Also known as **Raja's Cup**):
Clearing Nut Tree, Kasmard, Licorice, Winter Cherry.

The herbs in Maharishi Coffee Substitute contain the following biologically active ingredients, some of which are antioxidants:

- Glycyrrhizin
- Bioflavonoids and their Glycosides
- Coumarin and Cinnamic Acid Derivatives
- Liquiritin and Isoliquiritin
- Alkaloids

Reference:

Hari M. Sharma, Atef N. Hanna, Ellen M. Kauffman, and Howard A.I. Newman. Inhibition of human low-density lipoprotein oxidation in vitro by Maharishi Ayur-Veda herbal mixtures. Pharmacology Biochemistry and Behavior, Vol. 43, No. 4, pp. 1175-1182, 1992.

6. **Ladies Rasayana:**
Hydechium spicatum, Cyperus rotundus, Andrographis paniculata, Berberis aristata, Tinospora cordifolia, Piper longum, Piper nigrum, Cedrus deodara, Curcuma longa, Piper chaba, Embelia ribes, Elettaria cardamomum, Cinnamomum zeylanicum, Cinnamomum tamala, Bambusa arundinacea, Zingiber officinale, Asphaltum, Balasmodendron mukul, Corallium rubrum, Ostea edulis.

Resources

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888-422-6748 (For Chemotherapy Patients - Amrit Health Institute)
719-260-5500 (Main Office Number)
Fax: 719-268-2693 (For Health Professionals)
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E-mail: admissions@mum.edu
Website: www.mum-edu/CMVM

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Website: www.tm.org

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