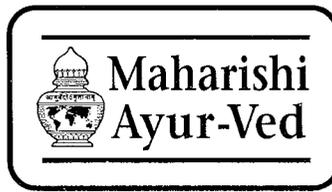




**Maharishi
Ayur-Ved**

Summary of Research Findings

<i>Cancer Research</i>	pg 5
<i>Research on Reduction of Chemical Toxicity</i>	pg 12
<i>Antioxidant Research</i>	pg 15
<i>Cardiovascular Research</i>	pg 28
<i>Diabetes Research</i>	pg 34
<i>Immunity Research</i>	pg 37
<i>Research on Neurophysiology and Intelligence</i>	pg 45
<i>Nutrition Insights</i>	pg 48
<i>Anti-Aging Research</i>	pg 49
<i>Research on Chronic Diseases</i>	pg 50
<i>Research on Organ Functions</i>	pg 52
<i>Research on Gene Regulation</i>	pg 53
<i>Research on Primordial Sound</i>	pg 54
<i>Research on the Maharishi Rejuvenation SM Program</i>	pg 55
<i>Research on the Transcendental Meditation [®] Program</i> ...	pg 62



Summary of Research Findings

Edited by

Hari Sharma, M.D., FRCPC

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Published by
Maharishi Ayur-Ved Products International, Inc.
1068 Elkton Drive
Colorado Springs, CO 80907

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Table of Contents

Cancer Research pg 5

1. Antineoplastic Properties of Maharishi-4 [MAK-4] Against DMBA-Induced Mammary Tumors in Rats
2. Antineoplastic Properties of Maharishi Amrit Kalash [MAK-5], An Ayurvedic Food Supplement, Against 7,12-Dimethylbenz(a)anthracene-Induced Mammary Tumors in Rats
3. Reduction of Metastases of Lewis Lung Carcinoma by an Ayurvedic Food Supplement [MAK-4] in Mice
4. Ayurvedic (Science of Life) Agents [MAK-4 and MAK-5] Induce Differentiation in Murine Neuroblastoma Cells in Culture
5. Chemopreventive Activity of Maharishi Amrit Kalash [MAK-4 and MAK-5] and Related Agents in Rat Tracheal Epithelial and Human Tumor Cells
6. Antioxidant Adjuvant Therapy Using Natural Herbal Mixtures [MAK-4 and MAK-5] During Intensive Chemotherapy: Reduction in Toxicity. A Prospective Study of 62 Patients
7. Effects of Ayurvedic Food Supplement MAK-4 on Cisplatin-Induced Changes in Glutathione and Glutathione-S-transferase Activity
8. Protective Effects of MAK-4 and MAK-5 on Adriamycin-Induced Microsomal Lipid Peroxidation and Mortality

Research on Reduction of Chemical Toxicity pg 12

1. Antioxidant Properties of Two Ayurvedic Herbal Preparations [MAK-4 and MAK-5]
2. In Vitro and In Vivo Inhibition of Microsomal Lipid Peroxidation by MA-631
3. Effect of Herbal Mixture Student Rasayana on Lipoxygenase Activity and Lipid Peroxidation

Antioxidant Research pg 15

1. Inhibitory Effects of Maharishi-4 [MAK-4] and Maharishi-5 [MAK-5] on Microsomal Lipid Peroxidation
2. Effect of Maharishi 4 [MAK-4] and Maharishi 5 [MAK-5] on Inflammatory Mediators—With Special Reference to Their Free Radical Scavenging Effect
3. 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]
4. In Vitro and In Vivo Inhibition of Microsomal Lipid Peroxidation by MA-631
5. Protective Effects of MAK-4 and MAK-5 on Adriamycin-Induced Microsomal Lipid Peroxidation and Mortality
6. In Vivo Effect of Herbal Mixture MAK-4 on Antioxidant Capacity of Brain Microsomes
7. Antioxidant Properties of Two Ayurvedic Herbal Preparations [MAK-4 and MAK-5]
8. Effect of Herbal Mixtures MAK-4 and MAK-5 on Susceptibility of Human LDL to Oxidation
9. Effect of Herbal Mixture Student Rasayana on Lipoxygenase Activity and Lipid Peroxidation
10. 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
11. The Antioxidant and Antiatherogenic Effects of MAK-4 in WHHL Rabbits
12. In Vitro Inhibition of Microsomal Lipid Peroxidation by MA-631, Student Rasayana (SR), Ladies Rasayana (LR), and Maharishi Coffee Substitute (MCS)

Cardiovascular Research pg 28

1. Effect of Herbal Mixtures MAK-4 and MAK-5 on Susceptibility of Human LDL to Oxidation
2. 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
3. The Antioxidant and Antiatherogenic Effects of MAK-4 in WHHL Rabbits
4. 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]
5. Maharishi Amrit Kalash (MAK-5) Prevents Human Platelet Aggregation
6. Indigenous Free Radical Scavenger MAK-4 and MAK-5 in Angina Pectoris. Is it Only a Placebo?

Table of Contents

Diabetes Research	pg 34
1. Hypoglycemic, Hypolipidemic and General Beneficial Effects of an Herbal Mixture MA-471	
Immunity Research	pg 37
1. Dose-Dependent Activation of Immune Function in Mice by Ingestion of Maharishi Amrit Kalash 5 (MAK-5)	
2. Immunomodulatory Effects of Maharishi Amrit Kalash 4 and 5 [MAK-4 and MAK-5] in Mice	
3. Immunomodulation by Maharishi Amrit Kalash [MAK-4] in Mice	
4. Enhanced Lymphoproliferative Response, Macrophage-Mediated Tumor Cell Killing and Nitric Oxide Production After Ingestion of an Ayurvedic Drug [MAK-5].	
5. Priming of Splenic Lymphocytes After Ingestion of an Ayurvedic Herbal Food Supplement [MAK-5]: Evidence for an Immunomodulatory Effect	
Research on Neurophysiology and Intelligence	pg 45
1. The Effect of the Maharishi Student Rasayana Food Supplement on Non-Verbal Intelligence	
2. Effect of Herbal Mixture Student Rasayana on Lipoxygenase Activity and Lipid Peroxidation	
3. In Vivo Effect of Herbal Mixture MAK-4 on Antioxidant Capacity of Brain Microsomes	
4. Antioxidant Properties of Two Ayurvedic Herbal Preparations [MAK-4 and MAK-5]	
5. Effect of Maharishi Amrit Kalash [MAK-5] on Brain Opioid Receptors and Neuropeptides	
Nutrition Insights	pg 48
1. Nutritional Insights From Maharishi Ayur-Veda	
Anti-Aging Research	pg 49
1. Influence of a Maharishi Ayur-Vedic Herbal Preparation [MAK-5] on Age-Related Visual Discrimination	
Research on Chronic Diseases	pg 50
1. The Maharishi Ayur-Veda Treatment of Ten Chronic Diseases—A Pilot Study	
Research on Organ Functions	pg 52
1. Effect of the Herbal Mixture MAK-4 on Organ Functions in Watanabe Heritable Hyperlipidemic (WHHL) Rabbits	
Research on Gene Regulation	pg 53
1. Effect of Maharishi Amrit Kalash (MAK-4) on mRNAs Coding for Hepatic Glycosyltransferases in the Rat	
Research on Primordial Sound	pg 54
1. Effect of Different Sounds on Growth of Human Cancer Cell Lines In Vitro	
Research on the Maharishi RejuvenationSM Program	pg 55
1. Improvement in Cardiovascular Risk Factors Through Panchakarma Purification Procedures	
2. Influence of Maharishi Ayur-Veda Purification Treatment on Physiological and Psychological Health	
3. Health Promotion With a Traditional System of Natural Health Care: Maharishi Ayur-Veda	
4. Selective Growth Inhibition of a Human Malignant Melanoma Cell Line by Sesame Oil In Vitro	
5. The Use of Sesame Oil and Other Vegetable Oils in the Inhibition of Human Colon Cancer Growth In Vitro	
Research on the Transcendental Meditation[®] Program	pg 62
1. A Randomized Controlled Trial of Stress Reduction for Hypertension in Older African Americans	
2. Cost-Effective Hypertension Management: Comparison of Drug Therapies With an Alternative Program	
3. Usefulness of the Transcendental Meditation Program in the Treatment of Patients With Coronary Artery Disease	
4. The Impact of the Transcendental Meditation Program on Government Payments to Physicians in Quebec	

Introduction

Maharishi Ayur-Ved 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 Ayur-Ved covers all facets of life, including mind (consciousness), physiology, behavior, and environment. It is prevention-oriented and emphasizes optimal health. It also provides effective treatment modalities for chronic ailments.

Maharishi Ayur-Ved 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. Thousands of doctors worldwide have been trained in Maharishi Ayur-Ved and have integrated various techniques of Maharishi Ayur-Ved into their practice. Maharishi Ayur-Ved clinics using the whole range of technologies are available in the U.S., Europe, Japan, Russia, Africa, South America, and India.

During the last 30 years there has been extensive research conducted on the various modalities of Maharishi Ayur-Ved. Over 500 studies have been carried out at more than 200 independent institutions and universities in 27 countries. In addition, there are thousands of published studies on the wideranging health benefits of Ayurvedic herbs. Herein is presented the latest research on Maharishi Ayur-Ved, focusing specifically on the studies conducted on Maharishi Ayur-Ved herbal formulas. This research demonstrates striking health benefits and profound possibilities for Maharishi Ayur-Ved in the health care field.

Maharishi Ayur-Ved herbal formulas nourish the natural structures and functions of the physiology rather than treating superficial symptoms, through the use of whole herbs which display the full range of biological intelligence. The ingredients of these herbal formulas function synergetically to maximize the health-promoting benefits.

The effectiveness of the Maharishi Ayur-Ved herbal preparations is assured by stringent quality control measures which include the following:

- 1) **Authentic Preparation** that meticulously follows the ancient Ayurvedic texts
- 2) **Expert Herbalists** trained in *dravyaguna*, identification of authentic plant species
- 3) **Organic Herbs** that are free of pesticides and chemical additives
- 4) **Standardized Potency** based on high-performance liquid and thin-layer chromatography
- 5) **Modern Manufacturing** with state-of-the-art equipment
- 6) **Tested Twice:** microbiology and metals analysis by two independent laboratories to meet strict U.S. standards.

Cancer Research

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

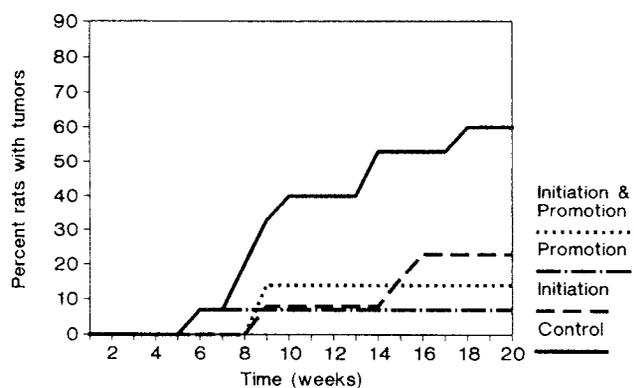


FIG. 1. Effect of 6% M-4-supplemented diet on tumor incidence. Tumor incidences in all groups were statistically analyzed using Chi-square test. C=60%, I=21%, P=7%, I&P=14%. I, P and I+P group were significantly different from C group ($p < 0.05$).

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)				Change in Tumor Volume (CM ³)
	1st Week	2nd Week	3rd Week	4th Week	
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.

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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.

Authors

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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.

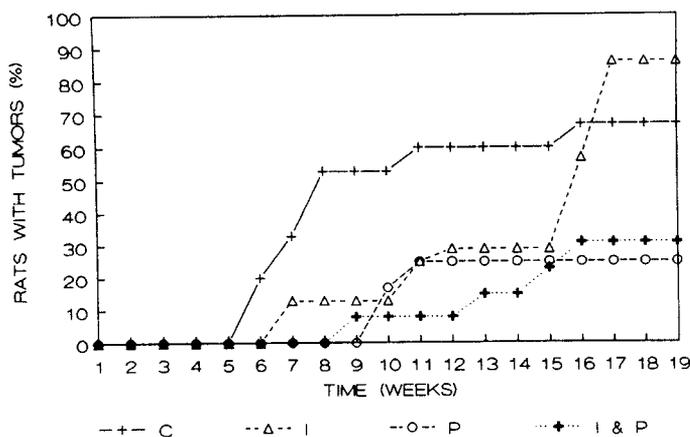


FIG. 2. Effect of 0.2% MAK-5-supplemented diet on tumor incidence. Tumor incidence in all groups was statistically analyzed using Chi-square test. The P and I+P groups were significantly different from C group ($p < 0.05$). Groups: C=control; I=initiation; P=promotion; I+P=initiation and promotion.

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)				CHANGE IN TUMOR VOLUME (CM ³)
	WEEK 1	WEEK 2	WEEK 3	WEEK 4	
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

CM³: 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

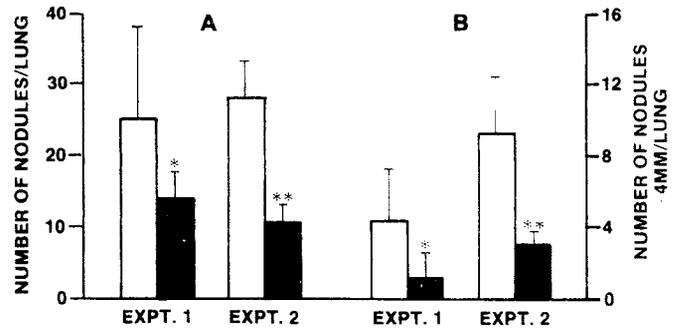


FIG. 1. Metastatic lung nodules (numbers/lung left side and size > 4 mm/lung right side) in animals on M-4-containing chow (Darkened Bars) and laboratory chow (Open Bars). *P < .01 & **P < .001.

4. Title

Abstract and figure reprinted by permission of the publisher from Nutrition Research, Vol. 12, pp. 51-61. Copyright 1992 by Elsevier Science Inc.

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

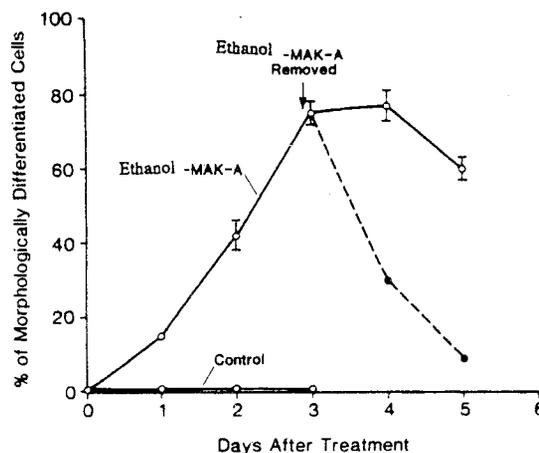


Fig. 2. Effect of an ethanol extract of MAK-A on morphological differentiation, as a function of treatment time. Ethanol-MAK-A (50 µg/ml) was added 1 day after plating. After 3 days of treatment, ethanol-MAK-A was removed and the number of morphologically differentiated cells was determined after 1 and 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 10^6 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.

Cancer Research *(continued)*

5. Title

Chemopreventive Activity of Maharishi Amrit Kalash [MAK-4 and MAK-5] and Related Agents in Rat Tracheal Epithelial and Human Tumor Cells

Publication

Proceedings of the American Association for Cancer Research, Vol. 32, p. 128, 1991 (Abstract).

Authors

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Summary

The rat tracheal epithelial (RTE) cell focus inhibition assay and the A427 human tumor cell anchorage independent assay were used to evaluate the chemopreventive potential of two medicinal Ayurvedic herbal mixtures, MAK-4 and MAK-5. A 1:1 aqueous:ethanol extract of MAK-4 inhibited benzo[a]pyrene-induced morphological transformation in the RTE assay by 27% and inhibited growth of the A427 tumor cells in soft agar by 51%. An aqueous extract of MAK-5 inhibited transformation in RTE cultures exposed to benzo[a]pyrene by 53%. These results suggest that MAK-4 and MAK-5 inhibit processes of neoplastic transformation. Compounds tested in these assays that are similar to the ingredients in MAK-4 and MAK-5 also show chemopreventive activity. These include curcumin, ferulic acid, catechin, bioflavonoids, retinoic acid, ascorbyl palmitate, and glycyrrhetic acid.

6. 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, cisplatin, 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.

7. 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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Conducted at

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**South Dakota State University, Brookings, SD

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 ($\mu\text{g/g}$ tissue)		GST ($\mu\text{mole/mg/min}$)	
	Liver	Kidney	Liver	Kidney
1 Control	11619 \pm 1574	4581 \pm 1125	1.91 \pm 0.5	1.47 \pm 0.2
2 Cisplatin	8899 \pm 1606*	2839 \pm 920*	1.13 \pm 0.2*	1.18 \pm 0.3*
3 M-4	10942 \pm 747	4495 \pm 264	1.98 \pm 0.4	1.62 \pm 0.1
4 Cisplatin & M-4	10635 \pm 1262**	4374 \pm 188**	1.86 \pm 0.4**	1.96 \pm 0.2**

*Significantly lower than control group ($P < 0.05$)

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

8. 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

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

*CDF₁ mice were treated with Adriamycin, 15 mg/kg, i.p. and animals were observed for four weeks for mortality.

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

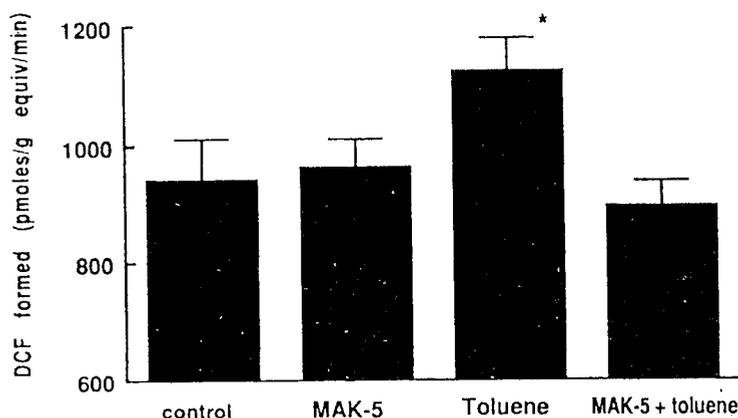


FIGURE 3

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

Research on Reduction of Chemical Toxicity *(continued)*

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.

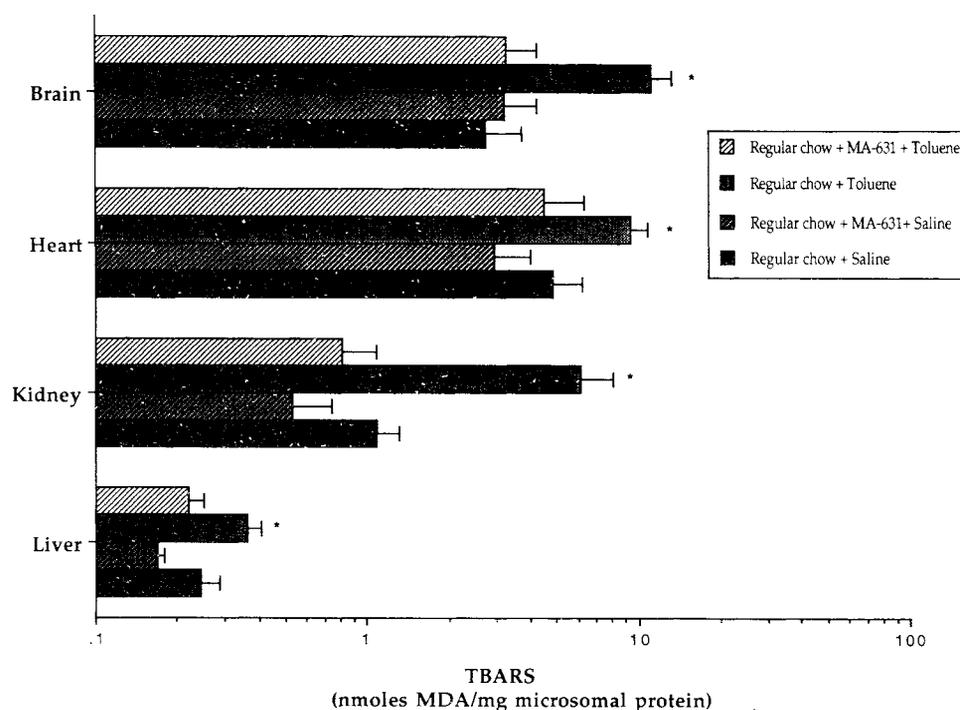


FIG. 3. Effect of in vivo pretreatment with MA-631 on toluene-induced microsomal lipid peroxidation. Animals were fed regular chow or regular chow supplemented with 2% MA-631 (w:w) for three weeks, then injected IP with toluene or a comparable volume of normal saline. Two hours after injection all animals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

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Research on Reduction of Chemical Toxicity (continued)

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 Neurophysiology and Intelligence.

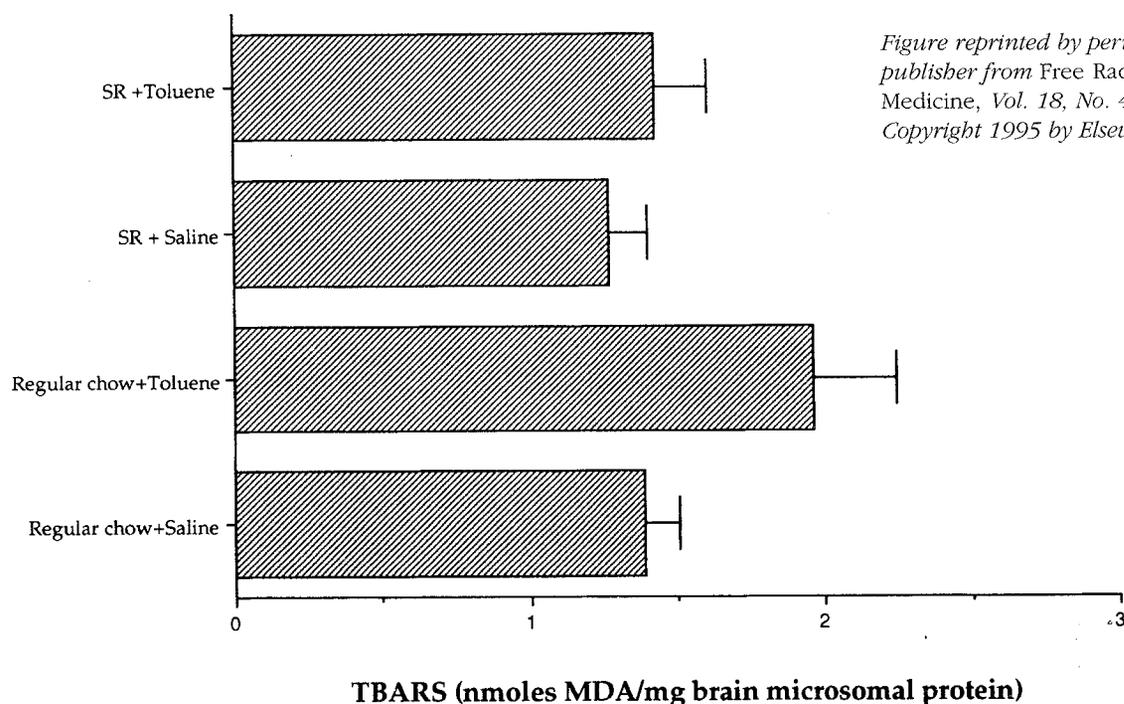


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Fig. 5. Effect of in vivo pretreatment with SR on toluene-induced brain microsomal lipid peroxidation. Animals were fed regular chow or regular chow supplemented with 2% (w:w) SR for 3 weeks, then injected intraperitoneally with toluene or a comparable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

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.

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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 superox-

Antioxidant Research (continued)

ide, 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.

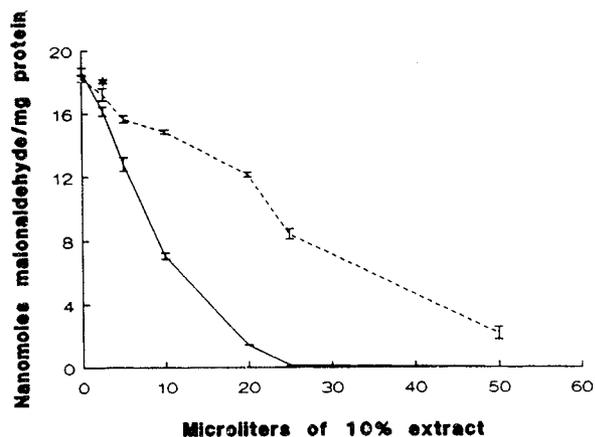


FIG. 1. Effect of M-4 (10% extract) on ascorbate-induced hepatic microsomal lipid peroxidation. The aqueous extract (—) or alcoholic extract (---) was added to the incubation mixture (total incubation volume = 2 ml) described in the Method section. Malonaldehyde values at each point represent the mean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

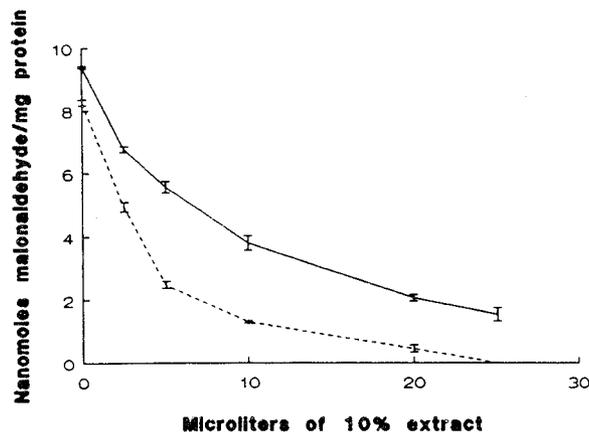


FIG. 4. Effect of M-5 (10% extract) on NADPH-stimulated hepatic microsomal lipid peroxidation. The aqueous extract (—) or alcoholic extract (---) was added to the incubation mixture (total incubation volume = 2 ml) described in the Method section. Malonaldehyde values at each point represent the mean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

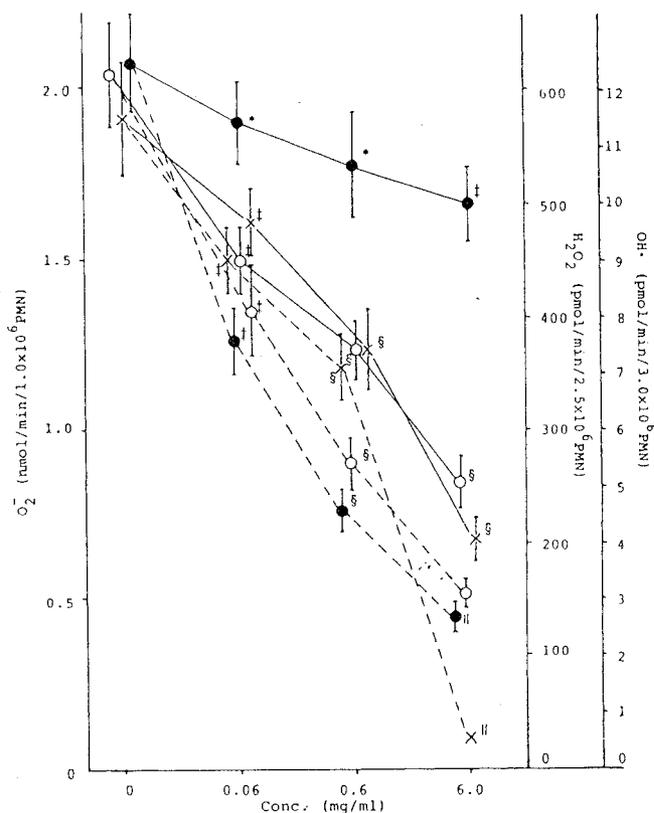


FIG. 2. Effect of MAK-5 on ROS generated by human neutrophils and in xanthine-xanthine oxidase system. Closed circle (●) denotes O_2^- (superoxide); open circle (○) H_2O_2 (hydrogen peroxide); and cross symbol (X) OH (hydroxy radical) levels. Solid line (—) denotes each ROS generated by neutrophils, and dashed line (-----) in xanthine-xanthine oxidase system. PMN denotes polymorphonuclear leukocytes. * $P < 0.05$ vs. control, † $P < 0.01$, § $P < 0.001$, || $P < 0.0001$.

Antioxidant Research (continued)

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.

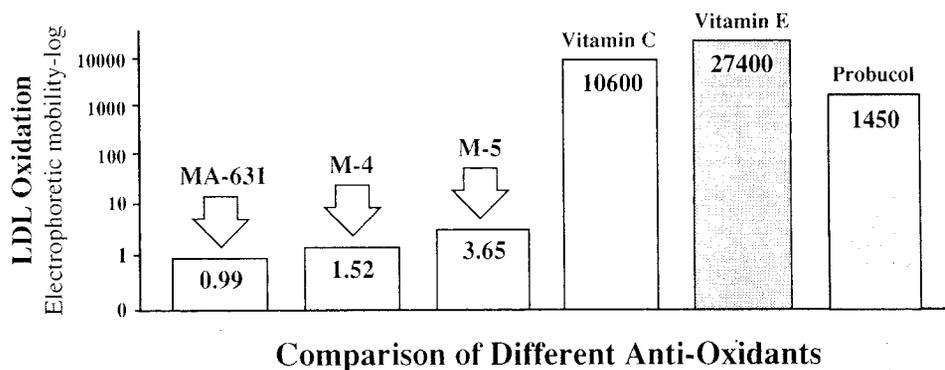
Conducted at

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% CO₂, 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.

Decreased Oxidation of LDL



MA-631, M-4, M-5 vs. vitamins C, E, and probucol, $p < .0001$.

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.

Antioxidant Research *(continued)*

TABLE 1
COMPARISON OF IC₅₀ (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 ± 0.613 × 10 ³	10.5 ± 1.49 × 10 ³
α-Tocopherol	19.6 ± 3.90 × 10 ³	26.0 ± 4.91 × 10 ³
Probucol	1.36 ± 0.658 × 10 ³	2.02 ± 0.089 × 10 ³

LDL (0.2 mg) was incubated in 95% air and 5% CO₂, 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 IC₅₀ (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 ± 0.678 × 10 ³	10.6 ± 1.70 × 10 ³
α-Tocopherol	23.2 ± 0.924 × 10 ³	27.4 ± 1.46 × 10 ³
Probucol	453 ± 42.1	1.45 ± 0.576 × 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.

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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 (IC₅₀) 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.

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Antioxidant Research (continued)

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.

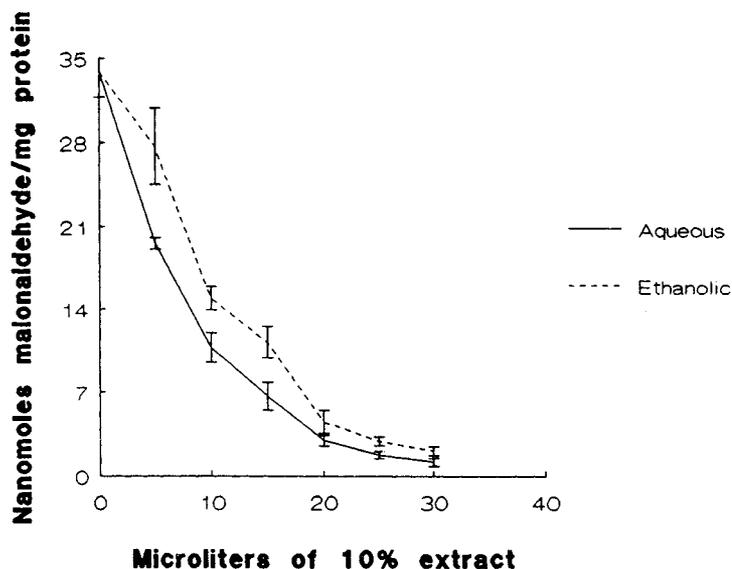


Figure 1
Effects of M-4 (10% extract) on Adriamycin-stimulated hepatic microsomal lipid peroxidation. Malonaldehyde values at each point represent the mean \pm SD of 3-6 determinations. The value for control incubations in the absence of Adriamycin was 22.75 ± 3.8 nanomoles malonaldehyde/mg protein.

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.

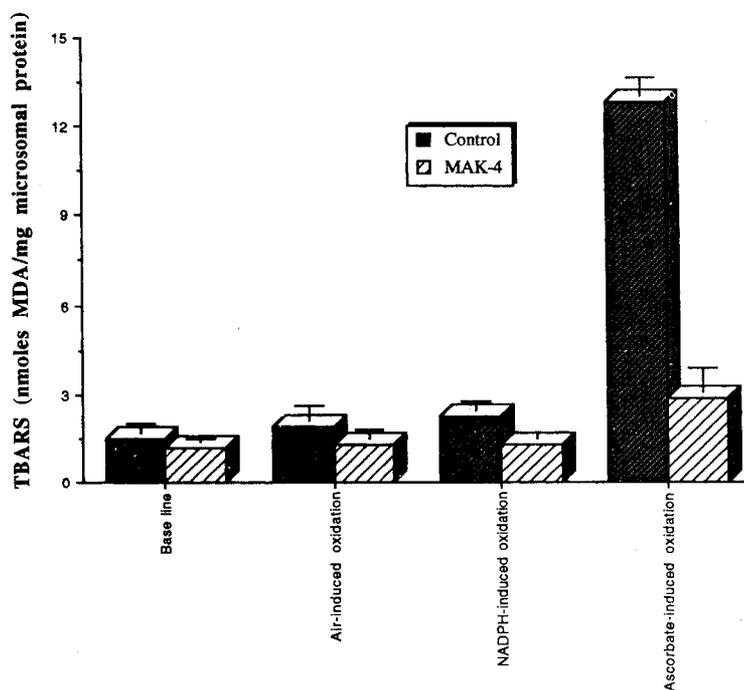


Figure 1

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 \pm S.E.

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

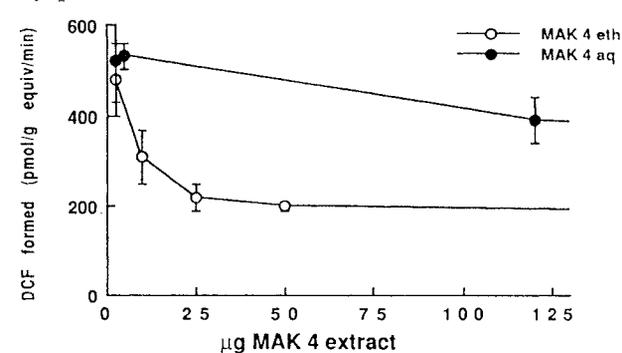


FIGURE 2

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

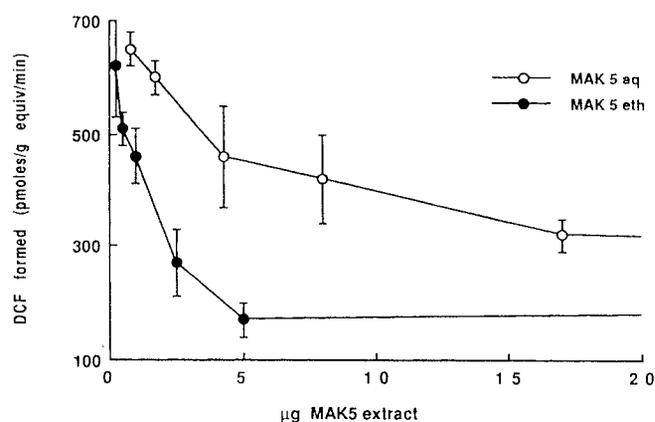


FIGURE 1

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

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.

Antioxidant Research *(continued)*

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% (IC₅₀) 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 IC₅₀ 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.

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 Neurophysiology and Intelligence for more information on this study.

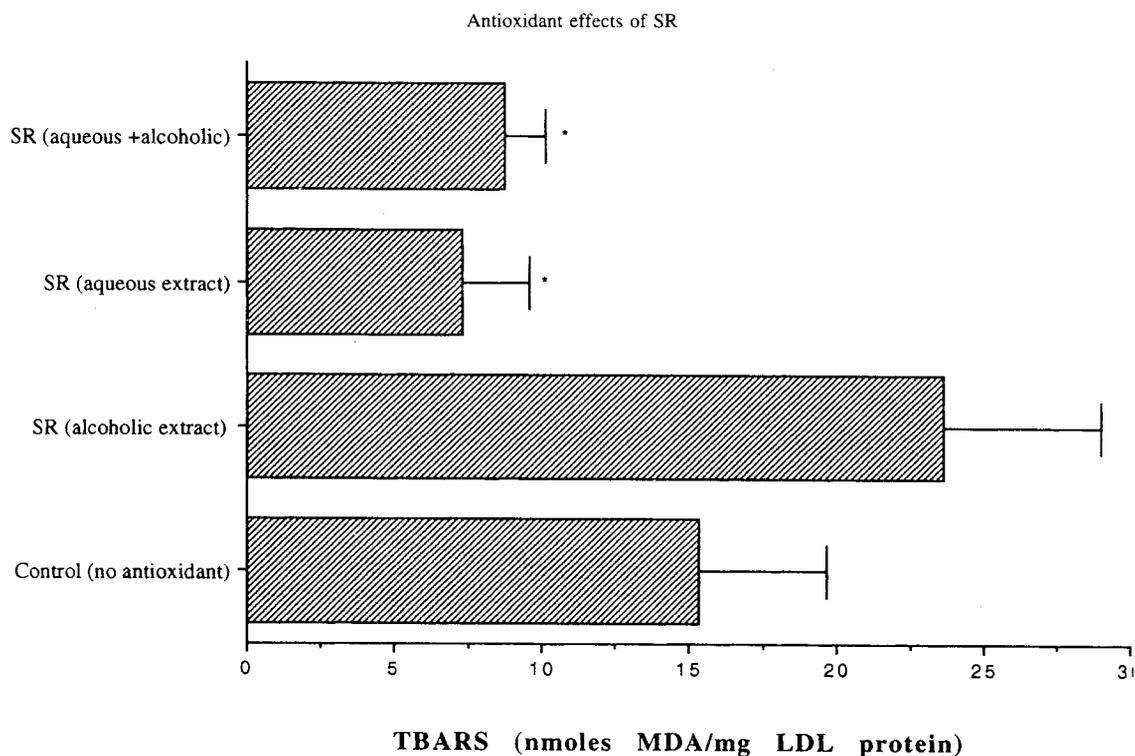


Fig. 1. Effect of simultaneous addition of alcoholic and aqueous extracts of SR on lipoxygenase-induced LDL oxidation. LDL was incubated with or without SLP and phospholipase A₂, in the presence or absence of the alcoholic extract (52 μ g) and/or the aqueous extract (640 μ g) of SR, at 37°C for 24 h. The degree of LDL oxidation was assessed by measuring TBARS. Values are mean \pm SD, $n = 3$. *Significantly lower ($p < 0.05$) than the control or the incubation mixture containing only the alcoholic extract of SR.

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

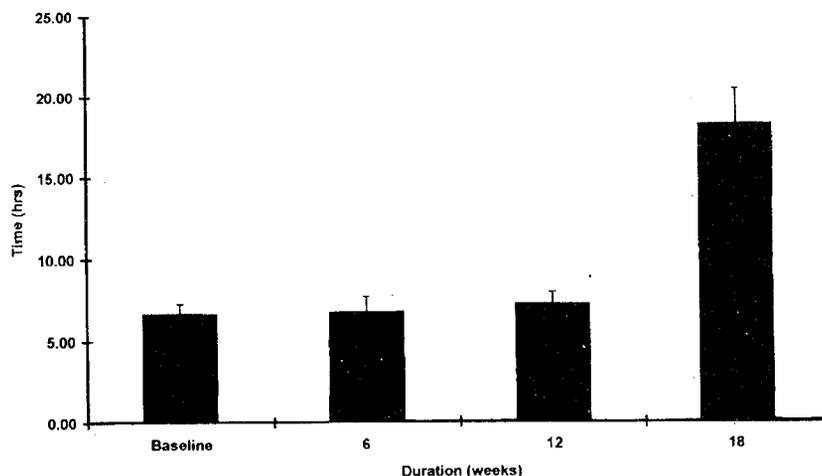
*Department of Internal Medicine and **Department of Pathology, College of Medicine, The Ohio State University, Columbus, OH

†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 \pm 0.19 (mean \pm standard error of mean), 6.77 hours \pm 0.31, 7.22 hours \pm 0.24, and 18.00 hours \pm 0.73, respectively, for Cu^{+2} -catalyzed LDL oxidation. Lag phases were 14.89 hours \pm 0.77, 13.33 hours \pm 0.50, 20.22 hours \pm 0.76, and 20.00 hours \pm 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 atherosclerosis.

Figure 2. Lag phase (mean \pm 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



Antioxidant Research (continued)

Figure 3. Lag phase (mean \pm 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

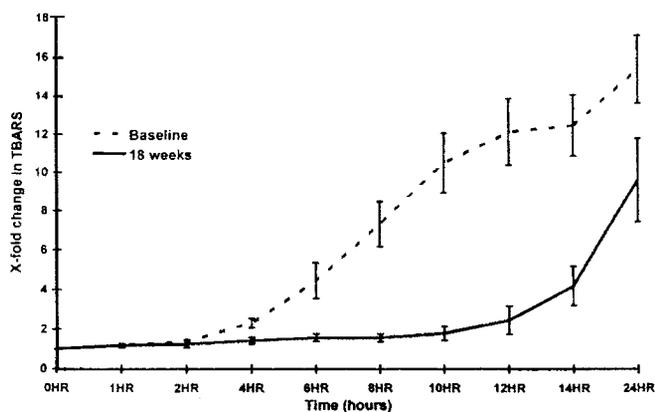
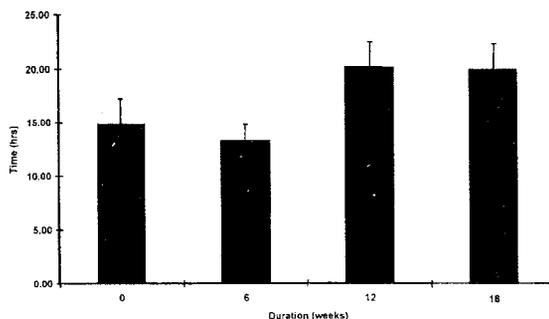


Figure 4. Plot depicting Cu^{+2} -induced low-density lipoprotein oxidation at baseline and after 18 weeks of treatment with MAK-4 and MAK-5. Y-axis represents x-fold change (mean \pm standard error of mean) in thiobarbituric acid-reactive substances.

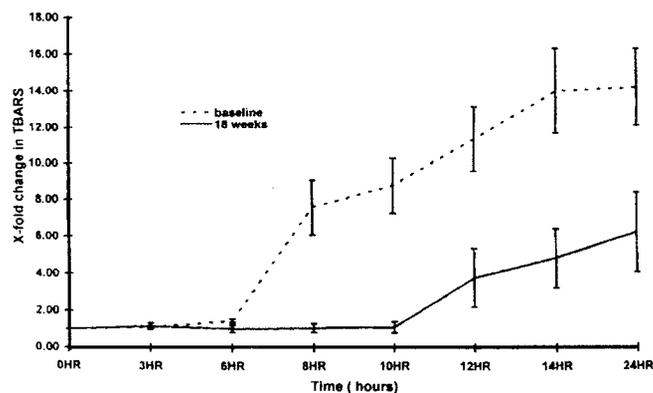


Figure 5. Plot depicting endothelial cell-induced low-density lipoprotein oxidation at baseline and after 18 weeks of treatment with MAK-4 and MAK-5. Y-axis represents x-fold change (mean \pm standard error of mean) in thiobarbituric acid-reactive substances.

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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

Antioxidant Research *(continued)*

visible plaque in the MAK-4 group ($22.5 \pm 4.2\%$, mean \pm SE) was significantly reduced ($p < 0.01$) compared to the control group ($47.6 \pm 6.8\%$, mean \pm 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.

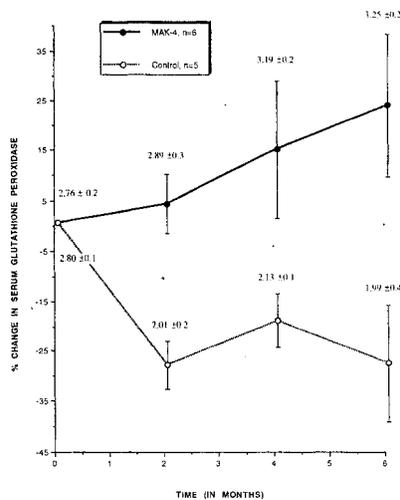


FIG. 3. Effect of MAK-4 on serum glutathione peroxidase activity in WHHL rabbits. Glutathione peroxidase is expressed as U/gm protein. Values are mean \pm SE. * $p < 0.05$.

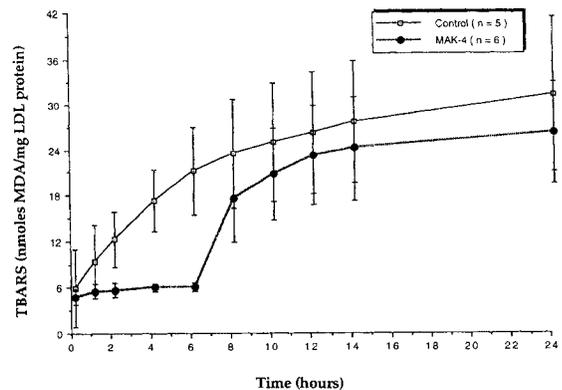


FIG. 4. Effect of MAK-4 on lag phase and propagation phase of cupric ion-catalyzed LDL oxidation at month 6, as assessed by measuring TBARS. LDL (0.2 mg) was incubated with or without $1 \mu\text{M}$ Cu^{+2} in a humidified environment of 95% air and 5% CO_2 at 37°C for various times. The degree of LDL oxidation was assessed by measuring TBARS. Values are mean \pm 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.

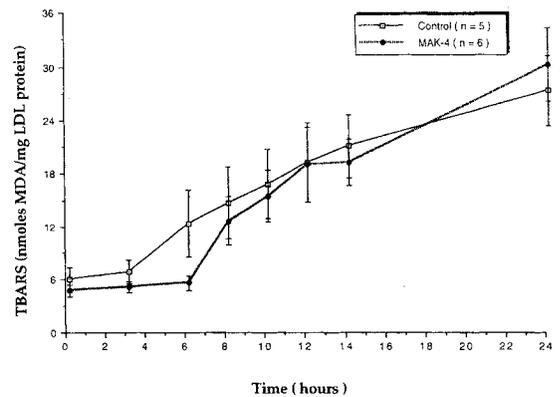


FIG. 5. Effect of MAK-4 on lag phase and propagation phase of endothelial cell-induced LDL oxidation at month 6. LDL (0.2 mg) was incubated with or without endothelial cells in a humidified environment of 95% air and 5% CO_2 at 37°C for various times. The degree of LDL oxidation was assessed by measuring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

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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.

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% (IC₅₀) 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 Cu²⁺-catalyzed LDL oxidation. Both the aqueous and alcoholic extracts inhibited free radical generation in a concentration-dependent manner. The IC₅₀ 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 Cu²⁺ 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 1a.

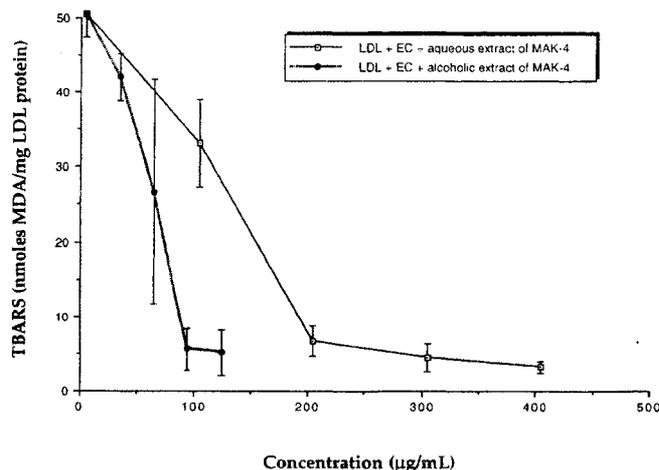
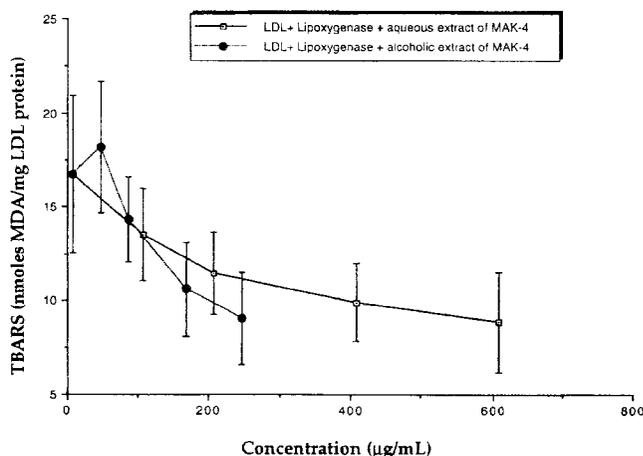
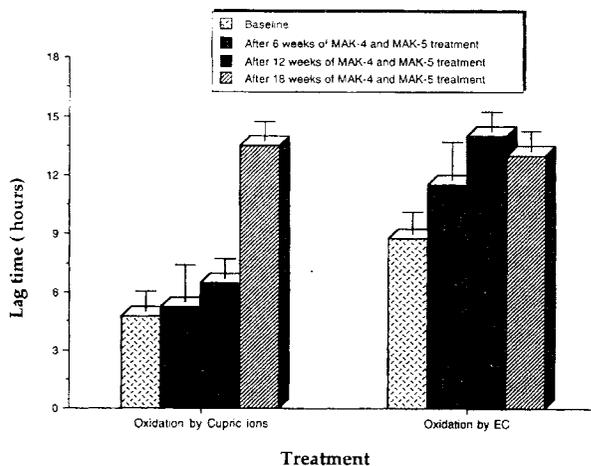


Figure 1b.



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 CO₂, 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.

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 CO₂. 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.

Cardiovascular Research *(continued)*

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 \pm 0.19 (mean \pm standard error of mean), 6.77 hours \pm 0.31, 7.22 hours \pm 0.24, and 18.00 hours \pm 0.73, respectively, for Cu^{2+} -catalyzed LDL oxidation. Lag phases were 14.89 hours \pm 0.77, 13.33 hours \pm 0.50, 20.22 hours \pm 0.76, and 20.00 hours \pm 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 atherosclerosis.

See Antioxidant Research for more information on this study.

3. Title

Abstract reprinted by permission of the publisher from The American Journal of the Medical Sciences, Vol. 314, No. 5, pp. 303-310. Copyright 1997 by Lippincott-Raven Publishers.

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.

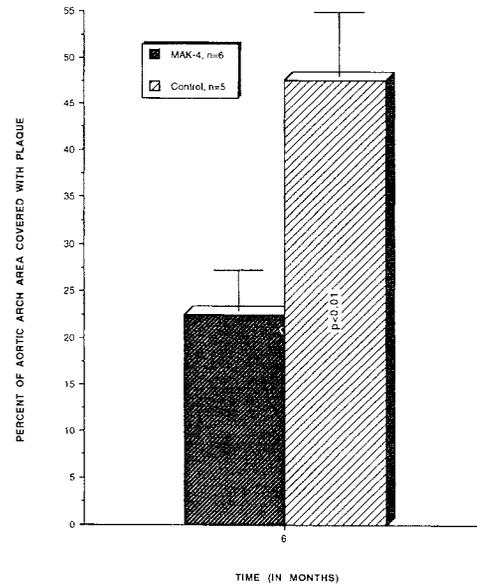


FIG. 8. Effect of MAK-4 on plaque formation on aortic arch in WHHL rabbits (22.5 ± 4.2% and 47.6 ± 6.8% for MAK-4 group and control group, respectively; values are mean ± SE). *p < 0.01

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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

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

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.

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

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

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.

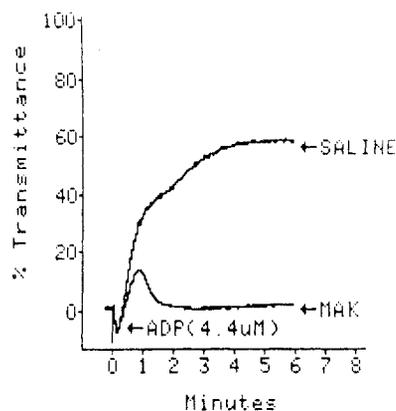


Fig. 1 - Effect of MAK on epinephrine induced platelet aggregation. This shows blockage of second phase of epinephrine induced aggregation.

Agonist	Dose	% Aggregation		Significance
		Control	MAK	
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.

Cardiovascular Research (continued)

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

* Department of Medicine, C.G.H.S., Jaipur, India

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

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

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

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.**

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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 A₁C 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.)

Diabetes Research (continued)

Table 1. Fasting and postprandial blood glucose and hemoglobin A₁C before and after MA-471.*

Group			Initial	After MA-471		
				3 months	6 months	9 months
A	Fast. glucose	n	15	15	15	13
		p value	9.28(± 1.22)	7.28 (± 1.11) < 0.001	6.77 (± 0.95) < 0.001	6.82 (± 0.82) < 0.001
	PP glucose	n	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 ₁ C	n	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	Fast. Glucose	n	30	30	30	25
		p value	6.43 (± 1.14)	5.90 (± 1.35)	5.54 (± 1.22)	5.70 (± 1.28)
	PP glucose	n	9.55 (± 1.07)	9.10 (± 1.02)	9.37 (± 1.24)	9.45 (± 1.36)
		p value				
	HBA ₁ C	n	7.0 (± 1.97)	7.1 (± 2.1)	7.8 (± 1.87)	7.6 (± 2.8)
		p value				
C	Fast. glucose	n	15	15	15	12
		p value	8.34 (± 1.21)	6.14 (± 1.07) < 0.001	6.01 (± 0.95) < 0.001	5.66 (± 0.79) < 0.001
	PP glucose	n	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 ₁ C	n	10.1 (± 2.5)	8.0 (± 1.7)	7.3 (± 1.8)	6.4 (± 1.5)
		p value			< 0.01	< 0.05
T O T A L	Fast. glucose	n	60	60	60	50
		p value	7.13 (± 1.27)	5.93 (± 1.01) < 0.001	5.75 (± 0.98) < 0.001	5.76 (± 1.02) < 0.001
	PP glucose	n	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 ₁ C	n	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 A₁C unit is percent. P values were derived by comparison with initial value. Fast. glucose = fasting glucose; PP glucose = Postprandial glucose; HBA₁C = hemoglobin A₁C.

Diabetes Research *(continued)*

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

Presenting complaint	Initial	After MA-471			Initial	After OHA		
	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	-	-

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 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 β -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.

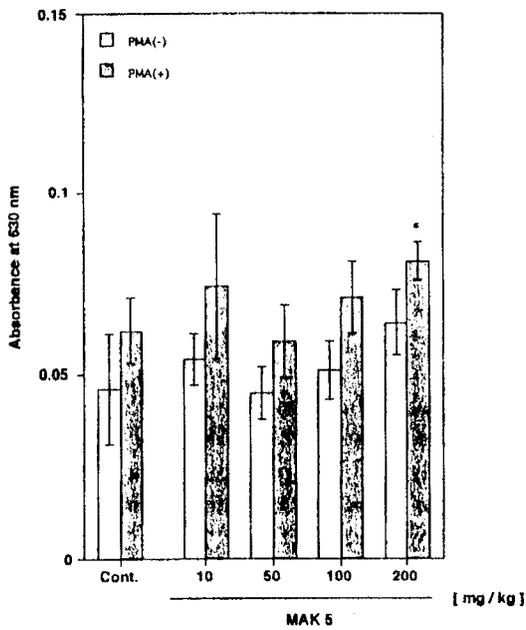


Fig. 2 Effects of Maharishi Amrit Kalash 5 (MAK 5) on superoxide anion (O_2^-) production of peritoneal macrophages in mice. Each value represents the mean \pm SE of triplicate determinations. * $p < 0.05$, compared with the controls. Cont., Control.

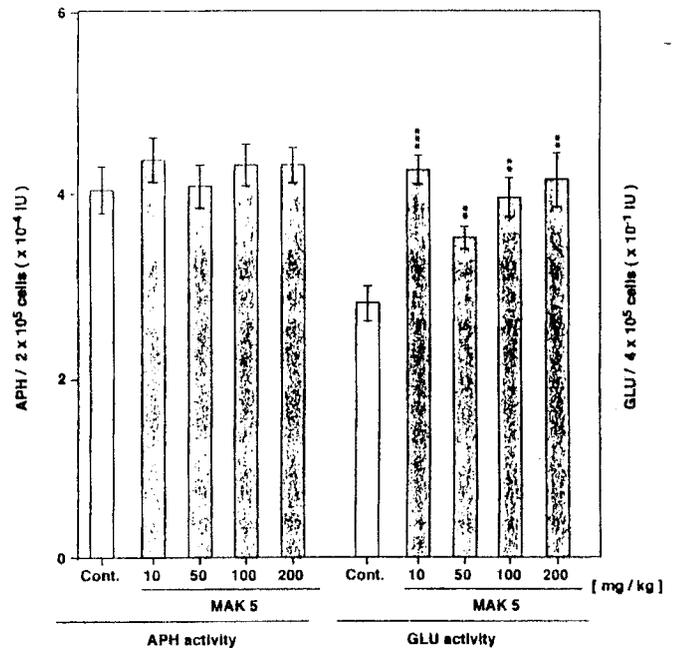


Fig. 3 Effects of Maharishi Amrit Kalash 5 (MAK 5) on acid phosphatase (APH) and β -glucuronidase (GLU) activities of peritoneal macrophages in mice. Each value represents the mean \pm SE of triplicate determinations. ** $p < 0.01$, *** $p < 0.001$, compared with the controls. Cont., Control.

Dose-Effects of MAK 5 on Immune Function

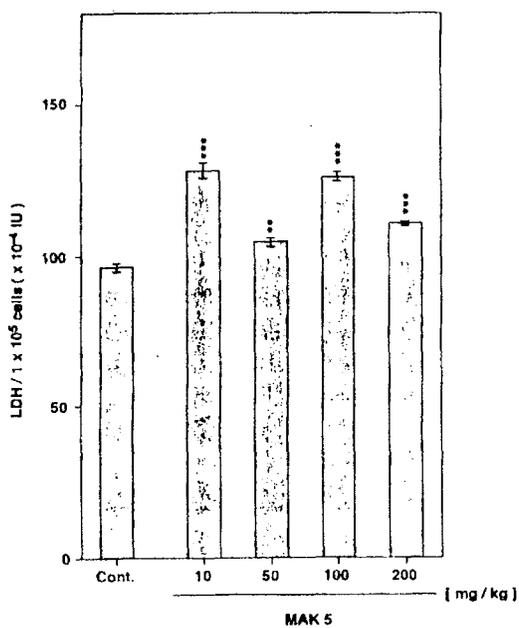


Fig. 4 Effects of Maharishi Amrit Kalash 5 (MAK 5) on lactate dehydrogenase (LDH) activities of peritoneal macrophages in mice. Each value represents the mean \pm SE of triplicate determinations. ** $p < 0.01$, *** $p < 0.001$, compared with the controls. Cont., Control.

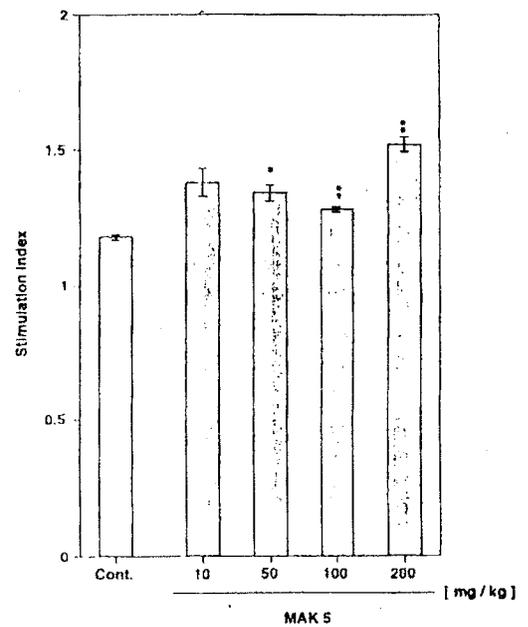


Fig. 5 Effects of Maharishi Amrit Kalash 5 (MAK 5) on proliferation of splenocytes induced by Con A in mice. Each value represents the mean \pm SE of 4 mice. * $p < 0.05$, ** $p < 0.01$, compared with the controls. Cont., Control.

Immunity Research

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.

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 (+)
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.

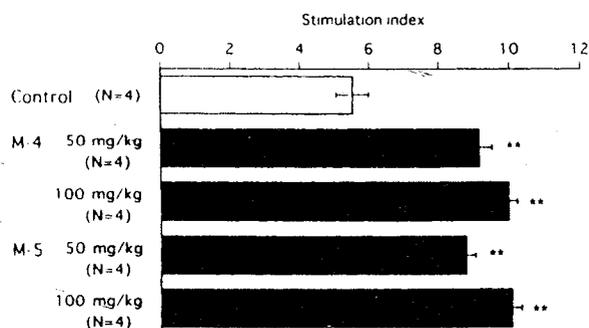


Fig. 2 Effects of M-4 and M-5 on proliferation of splenocytes induced by Con A in mice.

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,* Hirotoishi Iwata, PhD,* Hiroshi Mori, PhD,** and Takuji Tanaka, PhD.†

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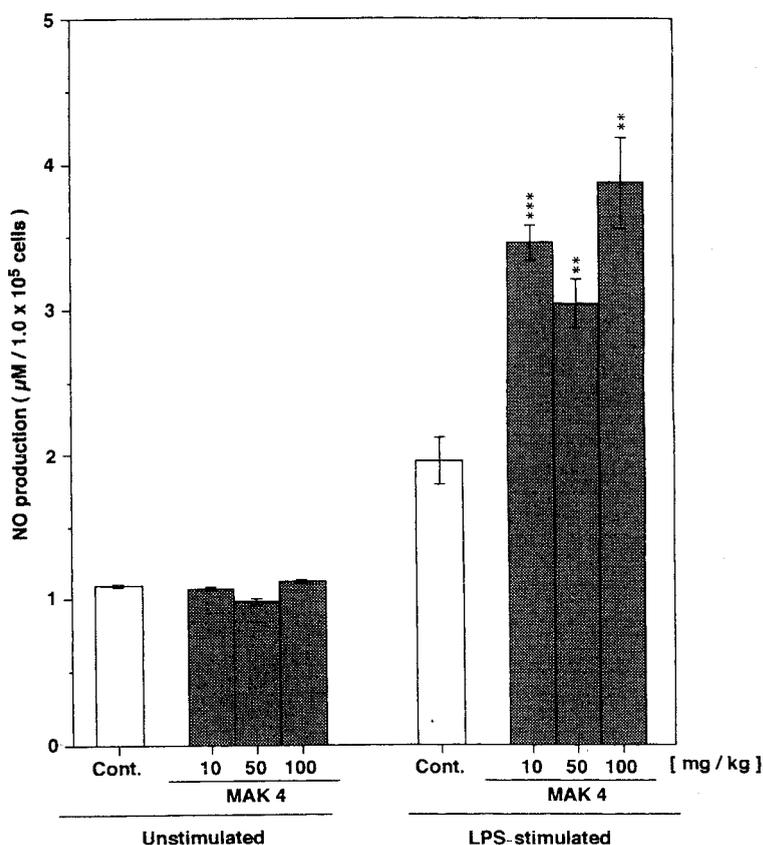
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Summary

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 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 ($p < 0.05$). Spleenocyte production of inter-

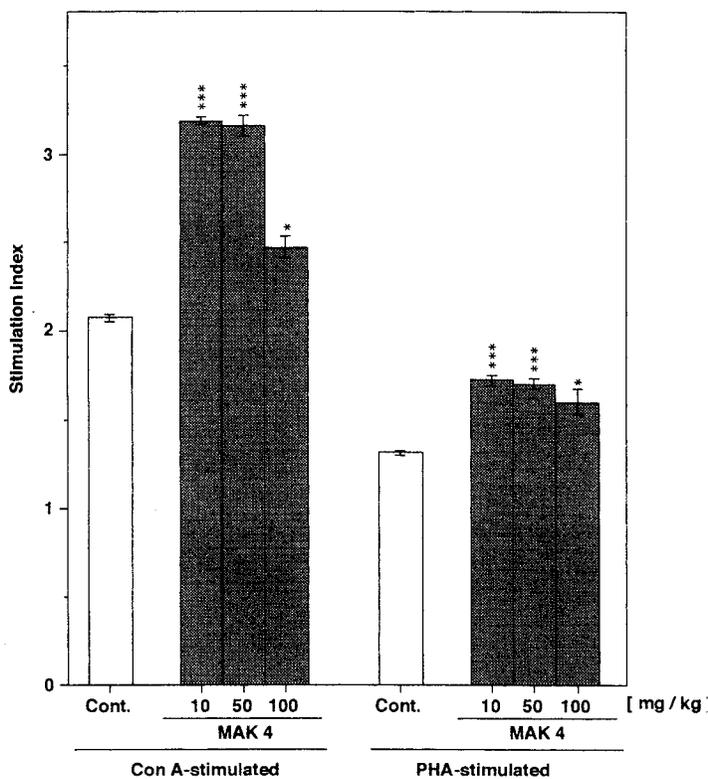
Figure 4 Effects of Maharishi Amrit Kalash 4 (MAK 4) on nitric oxide (NO) production by peritoneal macrophages cultured for 24 hours in mice.



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

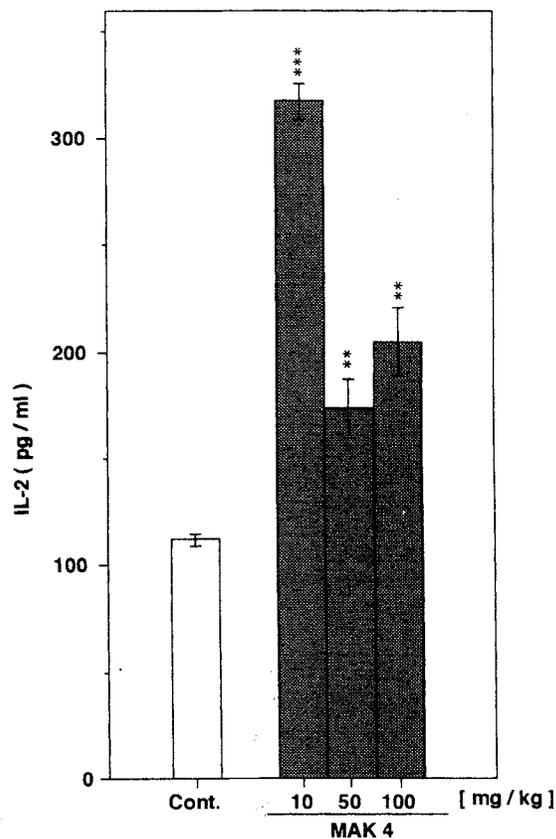
leukin-2 (IL-2) stimulated by Con A in the MAK-4 treated mice at all doses was significantly increased ($p < 0.01$). MAK-4 treated mice at the dose of 10 mg/kg had the highest IL-2 production by splenocytes. MAK-4 at any of the doses used did not enhance spontaneous NO production, spontaneous splenic 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 \pm 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 \pm SE of mice. ** $p < 0.01$, *** $p < 0.001$, compare with the control group (Cont.).

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 [³H] 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 [⁵¹Cr] 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.

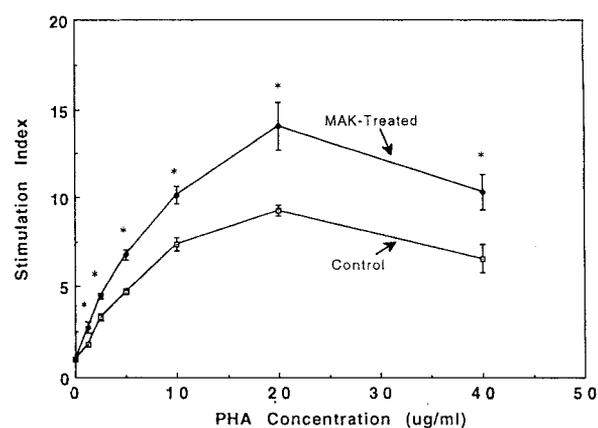


Figure 1. Effect of MAK treatment on PHA-induced splenic lymphocyte proliferation. The lymphoproliferative response to PHA was determined by the *in vitro* [³H]-thymidine uptake assay as described. Stimulation index is the ratio of PHA-induced [³H]-thymidine uptake to the unstimulated basal uptake. Each value given is the mean \pm 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 $p < 0.05$.

Immunity Research *(continued)*

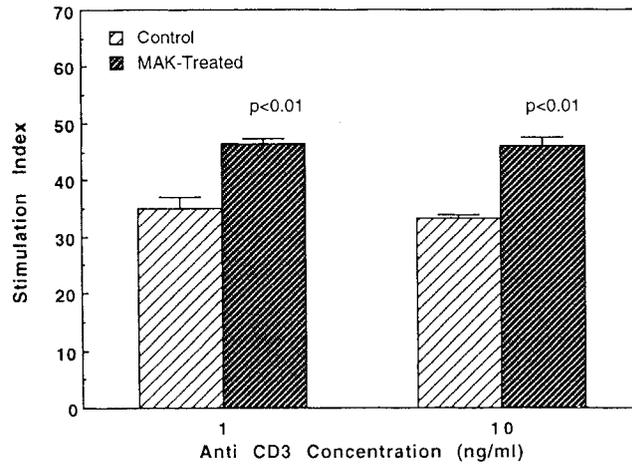


Figure 2. Effect of MAK treatment on anti CD3-induced splenic lymphocyte proliferation. The lymphoproliferative response to anti-CD3 was determined by the in vitro ^3H -thymidine uptake assay as described. Stimulation index is the ratio of anti-CD3-induced ^3H -thymidine uptake to the unstimulated basal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

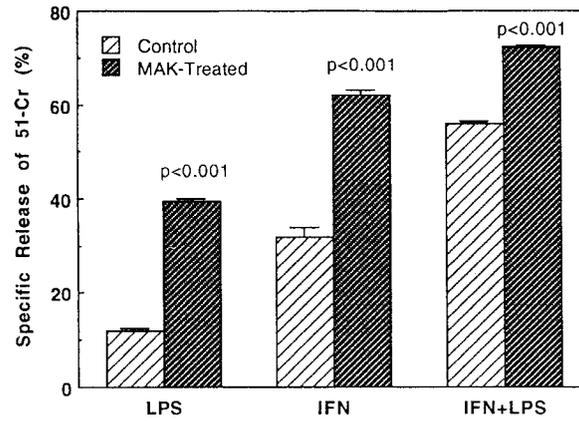


Figure 3. Effect of MAK treatment on macrophage-mediated tumor cell killing. Macrophage-mediated tumor cell killing was assayed by monitoring the release of ^{51}Cr from radiolabeled P815 mastocytoma cells (tumor targets) in an 18 hour co-culture. Concentrations of the activators used were: LPS, 1 $\mu\text{g}/\text{ml}$;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

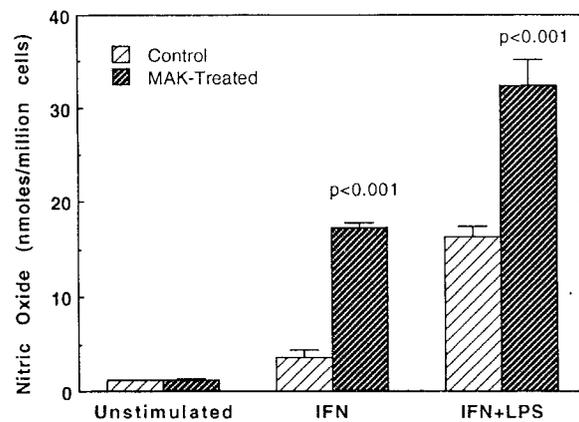


Figure 4. Effect of MAK treatment on nitric oxide production by macrophages. Production of nitric oxide by macrophages was assayed by monitoring nitrite content in the culture supernatants after 24 hour culture. Concentrations of the activators used were: LPS, 1 $\mu\text{g}/\text{ml}$; IFN, 100 units/ml.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

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.

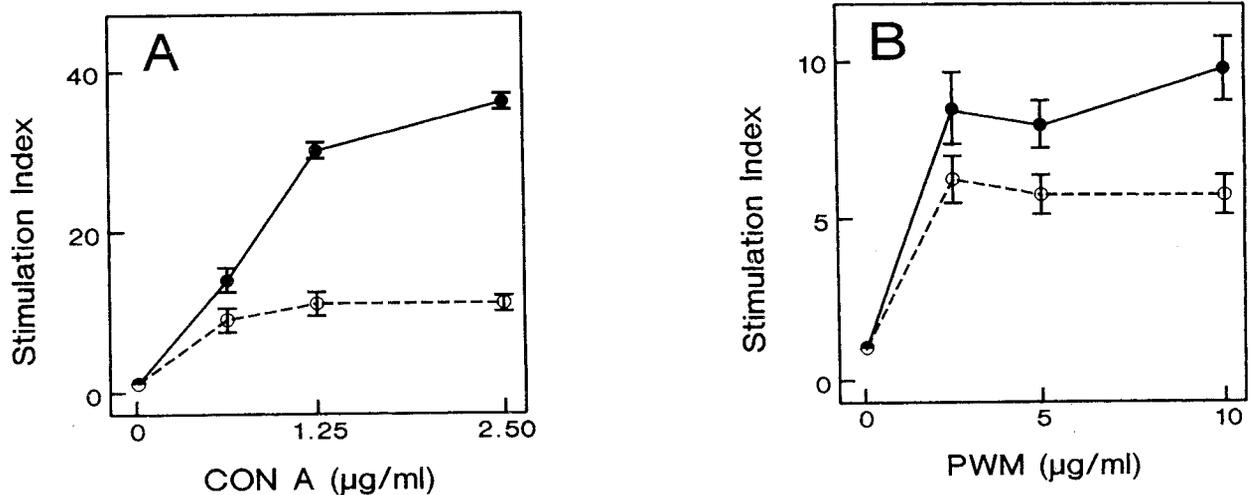


Figure 1

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 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)

Groups	N	Pretest		Posttest		Change	
		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.

Abstract and table reprinted from Personality and Individual Differences, Vol. 15, No. 5, pp. 599-602, Copyright 1993, with permission from Elsevier Science Ltd, The Boulevard, Langford Lane, Kidlington OX5 1GB, UK.

2. 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

Research on Neurophysiology and Intelligence *(continued)*

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.

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.

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.

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 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.

Table 2 Effect of MAK on Plasma Neuropeptides 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.

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

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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.

Anti-Aging Research

1. 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.

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, $p=0.12$).

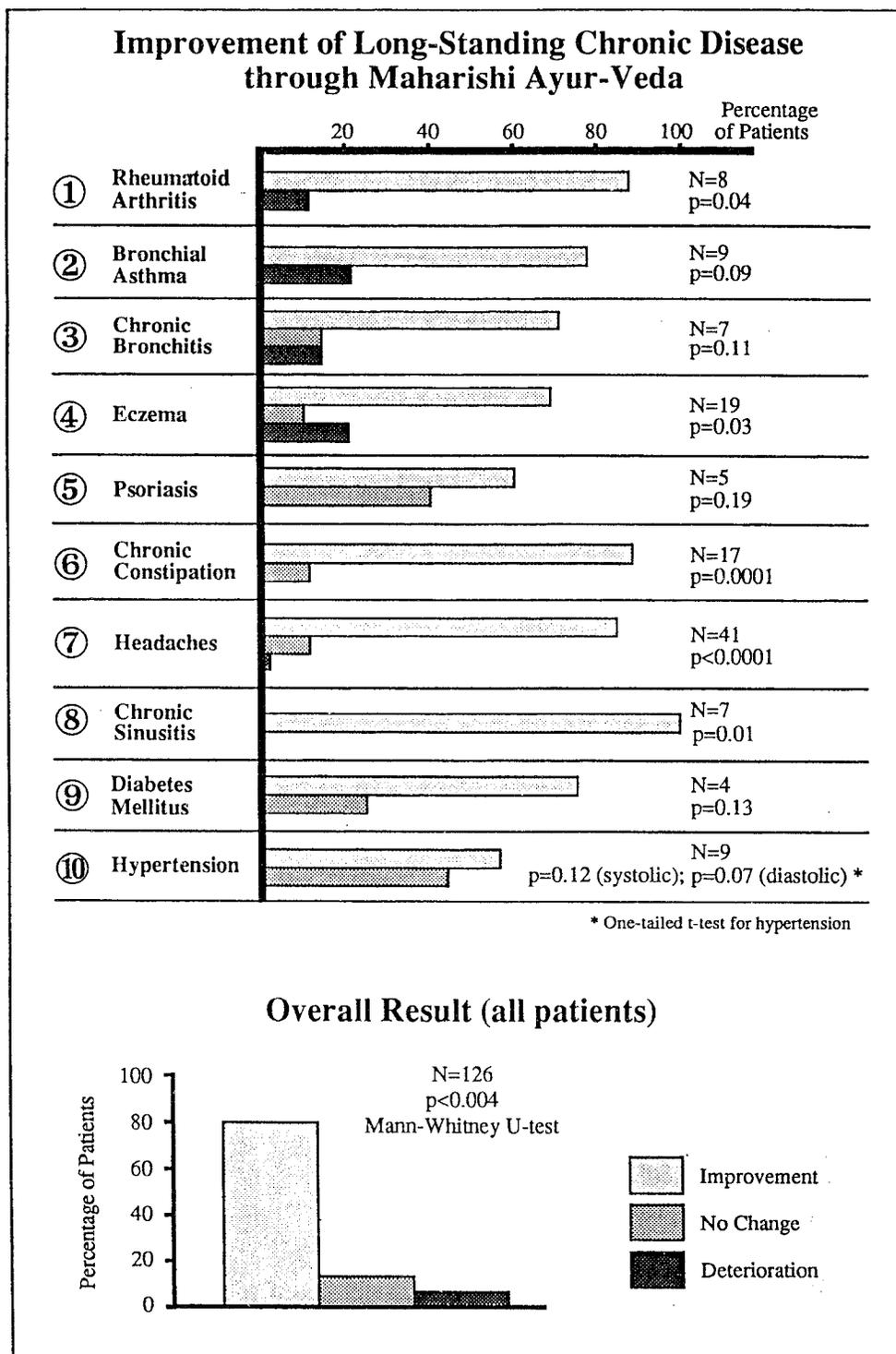
Ten subjects could be declared cured during the research period. Of the 35 participants who had medication prescribed by their family doctor or specialist, 14 (40%) could reduce their dose or could even stop the medication. The Maharishi Ayur-Veda preparations were tolerated well by 95% of the patients.

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 treat-

ment 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



Research on Organ Functions

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

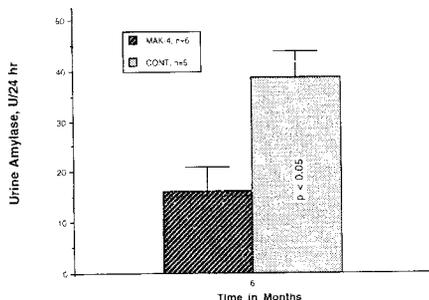


Figure 2

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

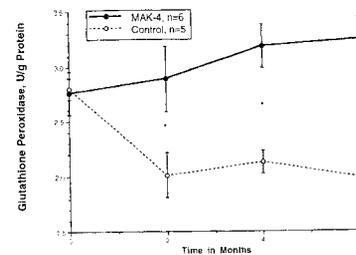


Figure 3

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

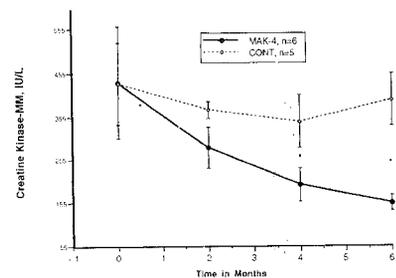


Figure 4

Effect of 6% MAK-4-supplemented diet on creatine kinase-MM isoenzyme in Watanabe Heritable Hyperlipidemic rabbits during a 6-month study period. CONT: controls. Values are mean \pm SE. * $p < 0.05$.

Research on Gene Regulation

1. Title

Effect of Maharishi Amrit Kalash (MAK-4) on mRNAs Coding for Hepatic Glycosyltransferases in the Rat

Publication

Proceedings of the American Association for Cancer Research, Vol. 33, p. 13, March 1992 (Abstract).

Authors

S. Rajalakshmi and R.K. Sharma.

Conducted at

Department of Pathology, University of Toronto, Toronto, Canada M5S 1A8

Summary

This study examined the effect of MAK-4 on genes coding for beta1,4 galactosyltransferase and beta-galactoside alpha-2,6 sialyltransferase in the rat liver. Rats maintained on a basal diet were given MAK-4 by gavage (4.1 mg/g b.w.) daily for 3 and 7 days. Hepatic poly-A RNA was isolated and analyzed for mRNA transcripts by Northern blot using cDNA probes. A dramatic increase in the levels of mRNA transcripts of both the genes was noticed in rats fed MAK-4 for 3 or 7 days. The effect of MAK-4 on hepatocarcinogenesis merits investigation in light of a previous study describing distinct changes of glycosyltransferases in the hepatic nodules from which cancer arises in the rat.

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			
No sound vs. Primordial sound			
Tissue/organ	Classification	Cell line	percent change
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.			

Research on the Maharishi RejuvenationSM 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), swedana (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).

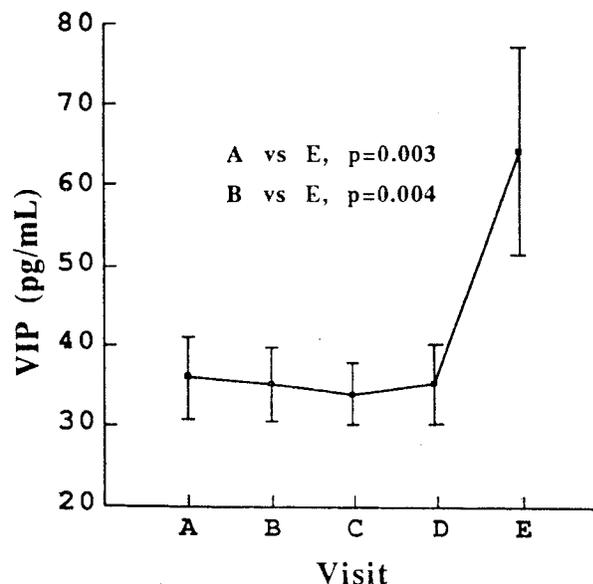


Figure. 1 Vasoactive intestinal peptide (VIP) in pg/mL for all subjects Means and Standard Error of the Mean (SEM) for each visit.

[§]Maharishi Panchakarma is another name for the Maharishi RejuvenationSM Program

Research on the Maharishi RejuvenationSM Program (continued)

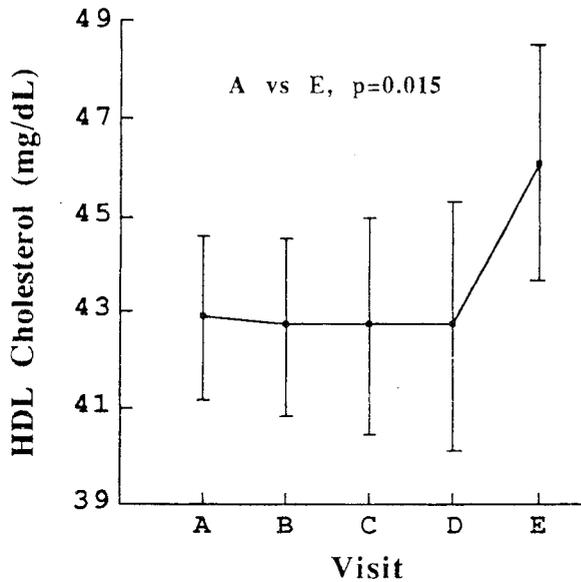


Figure 3 HDL cholesterol in mg/dL for those subjects (n=13) whose initial values at A were <50 mg/dL. Means and SEM for visit.

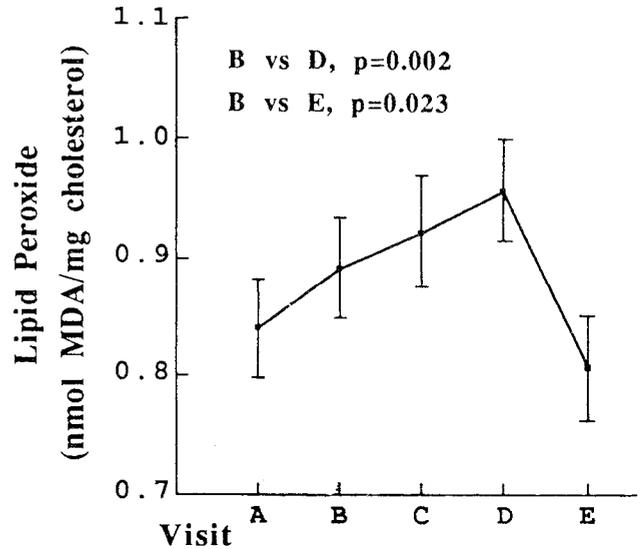


Figure 4 Lipid peroxide in nmoles of malondi - aldehyde/mg cholesterol for all subjects (n=27). Means and SEM for each visit.

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	
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

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

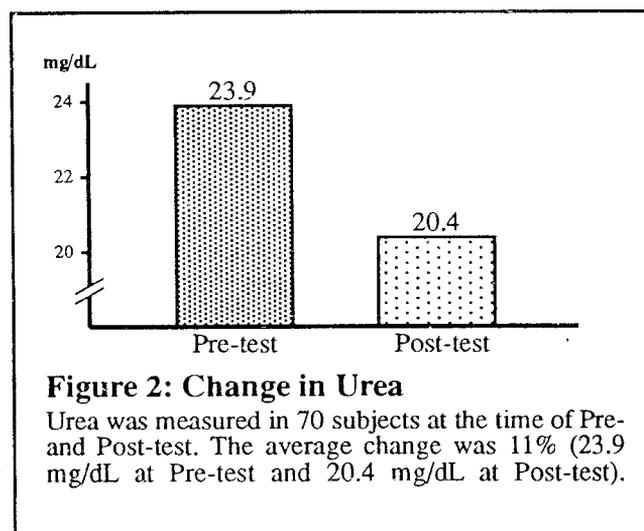
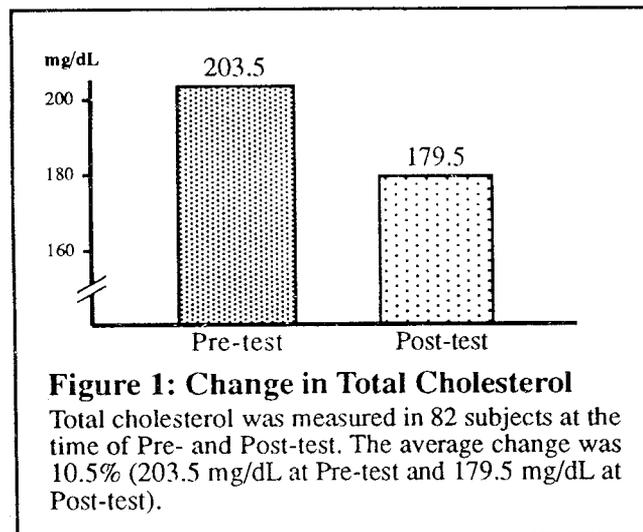
Albert-Ludwigs University, Freiburg, Germany

Summary

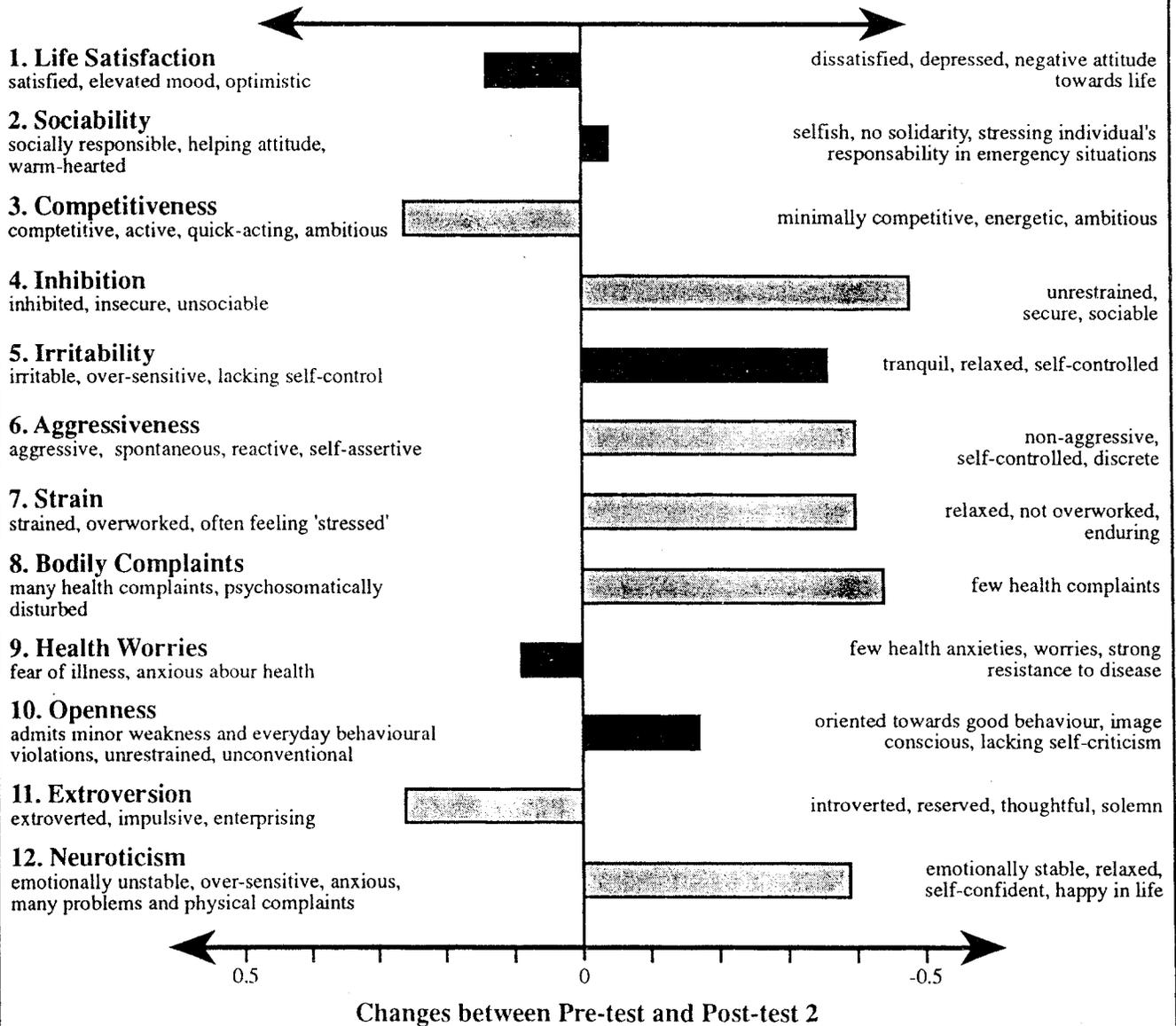
Maharishi Panchakarma[§], one of the many aspects of Maharishi Ayur-Veda, aims at purifying and balancing the physiology. This therapy includes herbalized oil massage (abhyanga), herbalized steam treatment (swedana), pouring of herbalized oil on the forehead (shirodhara), medicated enemas (basti), laxative 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, triglyc-

Research on the Maharishi RejuvenationSM Program *(continued)*

erides, 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 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.

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

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

**Department of Management and Public Affairs, Maharishi International University, Fairfield, IA 52556

† MAH Government Ayurveda Hospital, Ahmedabad, Gujarat, India

††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 RejuvenationSM Program

Research on the Maharishi RejuvenationSM Program (continued)

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.

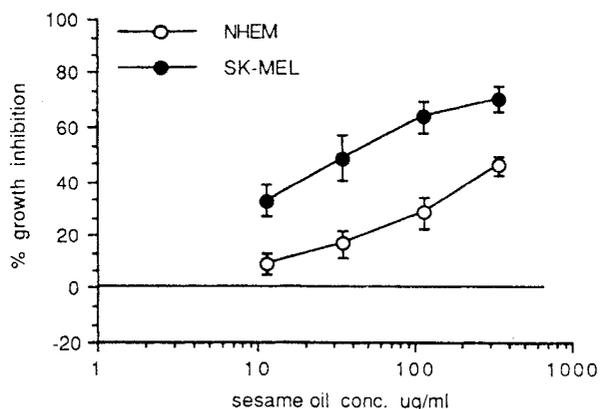


Fig. 2 Growth inhibiting effect of whole undigested sesame oil on the (SK-MEL ●) human malignant melanoma and (NHEM ○) normal human epidermal melanocytes. Dosage range was 10, 30, 100 and 300 $\mu\text{g/ml}$ plotted on logarithmic scale. All cells seeded at 1×10^4 per cm^2 (or 4×10^4 per well) in 12-well 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. $F(1, 11) = 13, p = 0.004$

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.

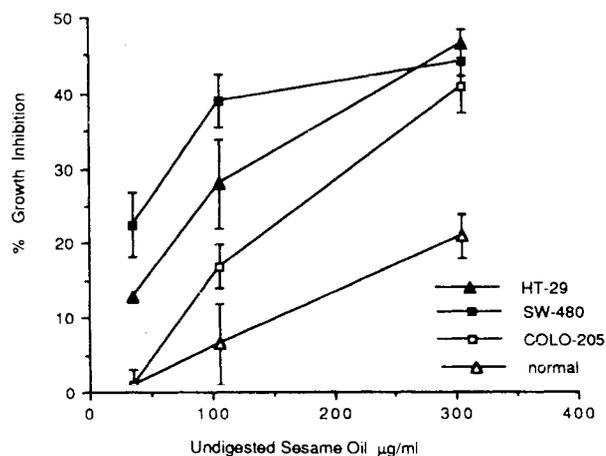


Figure 3. Growth inhibiting effect of whole undigested sesame oil at doses of 30, 100, 300 µg/ml on the growth rate of three human colon adenocarcinoma and one normal human colon cell line. Each point represents the mean and SEM of four experiments.

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 Staggars,** 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 ≤ 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 approximately twice as effective as progressive muscle relaxation. Long-term effects and generalizability to other populations require further evaluation.

Research on the Transcendental Meditation® Program (continued)

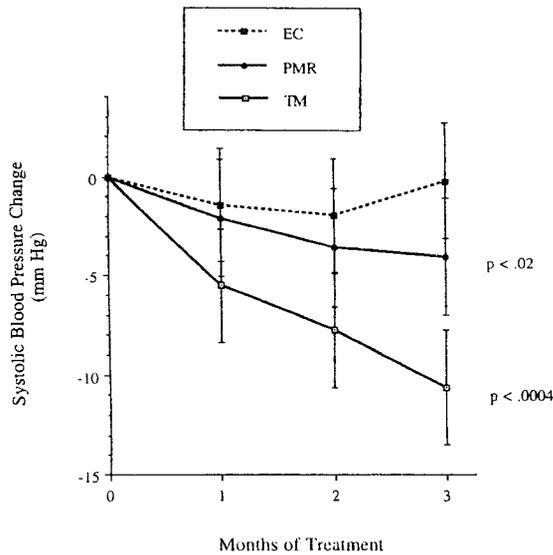


FIG 1. Line graph shows mean changes in clinic systolic pressure over 3 months (follow-up minus baseline) with SEM. Probability values are for repeated-measures ANCOVA comparing each experimental group (TM and PMR) with control (EC). TM indicates Transcendental Meditation (n=36); PMR, progressive muscle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

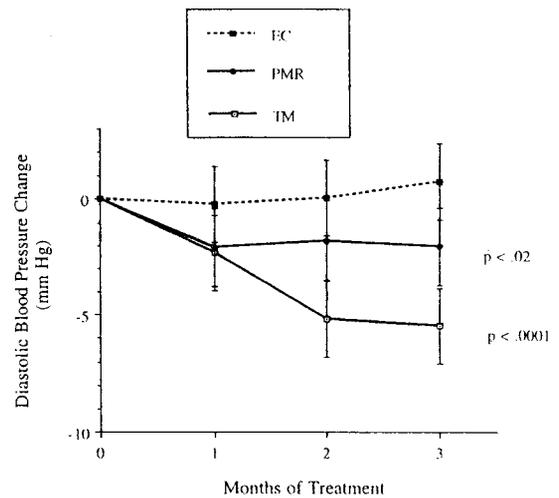


FIG 2. Line graph shows mean changes in clinic diastolic pressure over 3 months (follow-up minus baseline) with SEM. Probability values are for repeated-measures ANCOVA comparing each experimental group (TM and PMR) with control (EC). TM indicates Transcendental Meditation (n=36); PMR, progressive muscle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

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

* Institute of Science, Technology and Public Policy, and

**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.

Research on the Transcendental Meditation® Program *(continued)*

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 anti-hypertensive 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.

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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

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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.

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Research on the Transcendental Meditation® Program *(continued)*

4. Title

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

Publication

American Journal of Health Promotion, Vol. 10, No. 3, pp. 208-216, 1996.

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Summary

Purpose. This study evaluated whether government medical payments in Quebec were affected by the Transcendental Meditation (TM) technique.

Design. This retrospective study used a pre- and postintervention design in which government payments for physicians' services were reviewed for 3 years before and up to 7 years after subjects started the technique. Payment data were adjusted for aging and year-specific variation (including inflation) using normative data. No separate control group was used; thus it is impossible to determine whether the changes were caused by the TM program or some other factor.

Subjects. A volunteer group of 677 provincial health insurance enrollees was evaluated. The subjects had chosen to practice the TM technique before they were selected to enter the study. The subjects (348 men, 329 women) had diverse occupations. Their average age was 38 years and ranged from 18 to 71 years at the start of the TM program.

Intervention. The TM technique of Maharishi Mahesh Yogi is a standardized procedure practiced for 15 to 20 minutes twice daily while sitting comfortably with eyes closed.

Setting. Province of Quebec, Canada.

Results. During the 3 years before starting the TM program, the adjusted payments to physicians for treating the subjects did not change significantly. After beginning TM practice, subjects' adjusted expenses declined significantly. The several methods used to assess the rate of decline showed estimates ranging from 5% to 7% annually.

Conclusions. The results suggest that the TM technique reduces government payments to physicians. However, because of the sampling method used, the generalizability of these results to wider populations could not be evaluated.

Research on the Transcendental Meditation® Program *(continued)*

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.
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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.

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For information on the Transcendental Meditation program:

Call: 1-888-532-7686
Or access website @ <http://www.tm.org>

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November, 2000

SUMMARY OF FINDINGS FROM STUDY EXAMINING THE EFFECTS OF WORRY FREE IN PATIENTS WITH GENERALIZED ANXIETY DISORDER

Background

Anxiety disorders are common psychiatric disorders often co-morbid with other psychiatric disorders. In the National Comorbidity Survey, Kessler and colleagues (1) interviewed over 8,000 subjects to determine the prevalence of DSM-III-R psychiatric disorders in the general population and found that 24.9% of the population reported having had any anxiety disorder in their lifetime. Anxiety disorders were also found to be slightly more prevalent than depressive disorders.

Today, herbal remedies are being encountered increasingly more often in psychiatric practice, where they are used to treat anxiety, depression and a variety of other psychiatric conditions (2,3, for review). As compared to depression, where dozens of clinical trials have been conducted on the efficacy of herbs such as St John's wort (2-5), fewer studies have examined the effects of herbal remedies on anxiety.

Ayurveda is the traditional system of medicine in India (6-8). The ayurvedic approach includes interventions of exercise, meditation/relaxation, diet and herbs. Studies on the medicinal aspects of the herbal components are being seen increasingly in the literature (9-13). Ayurvedic formulas contain whole herbs not isolated ingredients of herbs and typically contain an herbal combination rather than a single herb. The combination includes herbs that target a specific area of health such as the mind, immunity or energy, that are chosen to increase the potency of the formula by improving the body's ability to assimilate the nutrients and that eliminate or minimize potential discomfort or side effects associated with a particular herb. This study was designed to examine the effectiveness of an ayurvedic herbal supplement formulated to reduce anxiety.

Patients and Methods

This was a randomized double-blind placebo controlled pilot study designed to examine the effects of an herbal supplement (Worry Free) on feelings of anxiety and on physiological responses to acute stressors in patients with DSM-IV diagnosed Generalized Anxiety Disorder (GAD). The Mini-International Neuropsychiatric Interview-Clinician Rated (MINI) (14) was used in order to establish the DSM-IV diagnosis of GAD. The MINI uses a brief structured interview approach to determine 17 Axis I disorders using DSM-IV and ICD-10 diagnostic codes. Given the high co-morbidity of depression and anxiety, subjects were excluded who had a major depressive episode within the previous 6 months. All subjects received a complete history and physical exam by a physician to rule out underlying physical illness.

Ten patients were randomized to either an herbal supplement group (N=5) or a placebo group (N=5). The treatment period was 3 months. Patients took 2 tablets b.i.d., in the morning and

evening. Prior to and following treatment the Hamilton Anxiety Scale (HAMA) was administered by a Clinical Psychologist (15). In addition, all patients underwent a laboratory stressor protocol where each gave two different 6-minute public speeches in a randomized order. One was a non-specific speech task where patients prepared and presented a speech on a hypothetical situation that was designed to elicit feelings of anxiety. The other speech was on the topic of a specific anxiety-provoking situation the patients had encountered within the previous 3 months. Prior to and immediately following both speeches, subjects completed the Spielberger State Anxiety Scale (SSAS) (16). Blood pressure and heart rate were assessed prior to and following each speech (Dinamap 1846SX automated monitor). In addition, salivary cortisol levels were assessed at rest and following the speech testing period. Salivary cortisol levels are a non-invasive way to assess blood free cortisol levels as free cortisol levels in saliva correlate well with levels of cortisol in plasma (17). For the cortisol assessment, saliva was sampled using a salivette device (Sarstedt, Sparks, NV). Cortisol levels were determined by a commercial RIA (Diagnostic Products Corporation, Los Angeles, CA).

Data were analyzed by repeated measures analysis of variance and t-test.

Results

Following the 3-month treatment period, 4 from the herbal supplement group and 2 from the placebo group no longer fit criteria for GAD diagnosis. In addition, subjects in the herbal supplement group showed a two fold greater decrease in HAMA ratings as compared with the placebo group [herbal supplement group, 21.0 (SD=7.8) at pre-randomization to 7.0 (SD=8.5) at post-testing; placebo group, 20.4 (SD=9.9) at pre-randomization to 13.6 (SD=9.7) at post-testing. ($p < 0.05$).

At pre-randomization, across all subjects, the non-specific and specific speeches led to significant increases in ratings of state anxiety. The specific speech tended to elicit greater increases in state anxiety ratings as compared to the non-specific speech. At post-testing, as compared to pre-randomization testing, subjects in the herbal supplement group showed a significantly greater decrease in state anxiety responses to the specific speech stressor [herbal supplement group 41.2 (SD=4.3) at rest to 54.6 (SD=8.7) post-speech at pre-randomization to 36.0 (SD=16.7) at rest to 39.8 (SD=17.6) post-speech at post-testing; placebo group 51.2 (SD=12.5) at rest to 52.8 (SD=7.5) post-speech at pre-randomization to 46.6 (SD=16.6) at rest to 50.2 (SD=11.5) post-speech at post-testing ($p < 0.018$). There were no significant group differences in state anxiety responses to the non-specific stressor [herbal supplement group 41.2 (SD=4.3) at rest to 45.2 (SD=9.0) post-speech at pre-randomization to 36.0 (SD=16.7) at rest to 38.0 (SD=18.2) post-speech at post-testing; placebo group 51.2 (SD=12.5) at rest to 56.6 (SD=5.6) post-speech at pre-randomization to 46.6 (SD=16.6) at rest to 49.4 (SD=16.3) post-speech at post-testing.

At pre-randomization, across all subjects, the non-specific and specific speeches led to significant increases in blood pressure and heart rate. The average increases in systolic and diastolic blood pressure were 14.5 mmHg and 8.9 mmHg respectively and in heart rate, 6.2 bpm. There were no significant differences between the groups at pre- or post-testing in blood pressure or heart rate responses to either speech.

Regarding cortisol, there was no significant effect of the speech tasks on salivary cortisol levels. However, cortisol levels decreased in the supplement group yet increased in the placebo group. Following 3 months of treatment, the mean salivary cortisol levels decreased 2.77 nmol/l (sd=3.2) in the supplement group (from 8.7 nmol (SD=5.7) to 6.0 nmol (SD=2.8) and increased 1.88 nmol/l (SD=1.61) in the placebo group (from 1.45 nmol (SD=1.3) to 3.33 nmol (SD=1.6) ($F(1,9)=8.17, p=0.021$).

There were no adverse effects reported by any of the patients, either from the herbal supplement or the placebo group.

Comment

The findings from this pilot study suggest that the ayurvedic herbal supplement was effective in reducing ratings of trait anxiety, as well as reducing ratings of stress-induced anxiety regarding a personal anxiety-provoking event. These data suggest that herbal supplement formulations may hold promise for reducing anxiety symptoms in clinical populations.

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