Prof. **Birkmayer**
Health Products

ENADA®
Extends Life-Span of Cells and Organs

ENADA

the only real Anti-Ageing product

What is ENADA – NADH ?

What is Anti-Aging ?

N. A. D. H.

- Nicotinamide
- Adenin
- Dinucleotide
- Hydride
- also known as reduced
- **C o e n z y m e - 1**

N A D H

is the

biological form of

HYDROGEN

The Rocket Fuel is :

Hydrogen + Oxygen = Explosion + Water

The Cell Fuel is:

NADH + Oxygen = Energy + H_2O + NAD

NADH can be regarded as the „human rocket fuel“

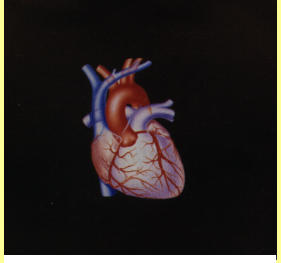
N A D H

occurs in

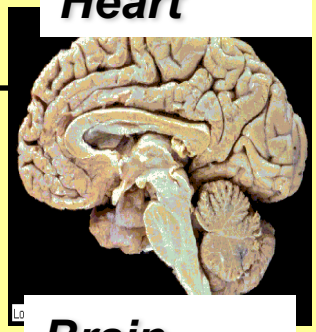
every living cell

NADH

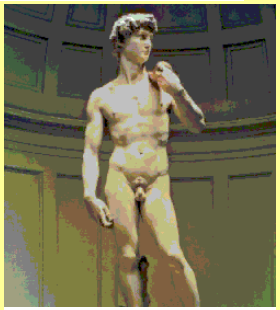
concentrations in human organs and tissues



Heart — **90 [mg/kg tissue]**



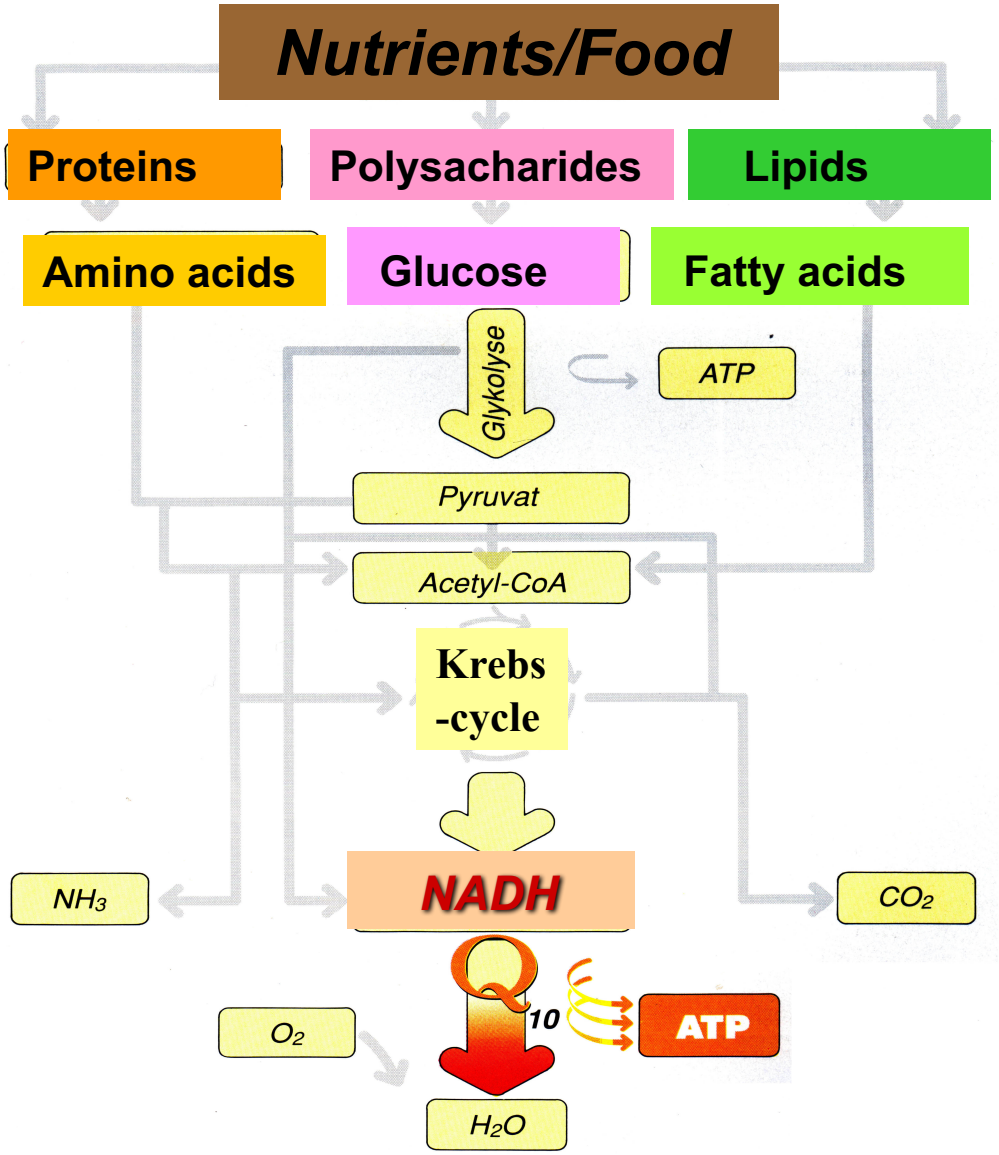
Brain — **40 [mg/kg tissue]**



Muscles — **50 [mg/kg tissue]**

Liver — **40 [mg/kg tissue]**

Erythrocytes — **8 [mg/kg tissue]**



The Mitochondrion Energy Plant
Adapted from Energy and Defense by Prof.Gian Paolo Littarru
Pub: Casa Editice Scientifica Internazionale, Rome Italy.

Biological functions of **ENADA**

- Fuel for cellular energy production
- Essential for cell and DNA repair
- Powerful Antioxidant
- Enhancer of immune system

ENADA is a very sensitive substance and easily degraded by oxygen, heat, light and acids

In order to make NADH bioavailable is has to be <u>stabilized</u> and transformed into an <u>orally absorbable</u> form

Prof. **Birkmayer**
Health Products

ENADA®

The only **stabilized**
food grade
oral absorbable form of

N.A.D.H.

51 patents for **ENADA®** have been issued worldwide

(7 formulation and 44 application patents
5 more patents are pending)

US005654288A

United States Patent [19]

Birkmayer

[11] **Patent Number: 5,654,288**

[45] **Date of Patent: Aug. 5, 1997**

[54] **STABLE NADH AND NADPH COMPOSITIONS FOR SUBLINGUAL ADMINISTRATION**

[75] Inventor: **Joerg G. D. Birkmayer**, Vienna, Austria

[73] Assignee: **Birkmayer Pharmaceuticals, Inc.**, New York, N.Y.

[21] Appl. No.: **632,373**

[22] Filed: **Apr. 10, 1996**

Related U.S. Application Data

[62] Division of Ser. No. 373,147, Jan. 17, 1995, Pat. No. 5,538,953.

[51] **Int. Cl.**[6] **A61K 31/70**

[52] **U.S. Cl.** **514/52**; 514/959

[58] **Field of Search** 514/52, 959

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,970,200	11/1990	Berkmayer et al.	514/52
5,019,561	5/1991	Birkmayer	514/52
5,332,727	7/1994	Birkmayer	514/52

FOREIGN PATENT DOCUMENTS

2057456	7/1996	Canada .
0 496 479 B1	7/1992	European Pat. Off. .
92/0275	12/1992	South Africa .

OTHER PUBLICATIONS

South African Patent 92/0275 is an English language counterpart of EPO 0 496 479 B1.

Primary Examiner—Theodore J. Criares
Attorney, Agent, or Firm—Kenyon & Kenyon

[57] **ABSTRACT**

NADH and/or NADPH is applied topically to the skin. It was surprising and totally unexpected to discover that NADH and NADPH are absorbed by the skin and penetrate the cutis to be taken up by the skin cells, where they stimulate certain enzymes which are essential for the energy production of the cells. The enzymes stimulated are principally the mitochondrial enzymes. The NADH and/or NADPH can be incorporated into a skin compatible cream, lotion or cosmetic. Liposomes are ideal vesicles for carrying the NADH and/or NADPH into the skin. In other embodiments of the invention, NADH and/or NADPH is administered nasally (e.g., as a liquid spray or a powder spray through the nostrils), sublingually (e.g., in the form of uncoated tablets inserted underneath the tongue) and rectally (e.g., in the form of suppositories) for known therapeutic effects (e.g., the treatment of Parkinson's disease).

9 Claims, No Drawings

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) **EP 0 697 859 B1**

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention of the grant of the patent:
04.06.1997 Bulletin 1997/23

(21) Application number: **94914734.2**

(22) Date of filing: **25.03.1994**

(51) Int. Cl.[6]: **A61K 9/36**, A61K 9/38, A61K 31/70, A61K 9/20, A61K 9/28

(86) International application number:
PCT/US94/03290

(87) International publication number:
WO 94/25007 (10.11.1994 Gazette 1994/25)

(54) STABLE, INGESTABLE AND ABSORBABLE NADH AND NADPH THERAPEUTIC COMPOSITIONS

STABILE, ORALE UND ABSORBIERBARE THERAPEUTISCHE ZUSAMMENSETZUNGEN VON NADH UND NADPH

COMPOSITIONS THERAPEUTIQUES PERORALES, STABLES ET ABSORBABLES DE NADH ET DE NADPH

(84) Designated Contracting States:
AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE

(30) Priority: **29.04.1993 US 55049**

(43) Date of publication of application:
28.02.1996 Bulletin 1996/09

(73) Proprietor: **Birkmayer Pharmaceuticals, Inc.**
New York, NY 10118 (US)

(72) Inventor: **BIRKMAYER, Joerg G.D.**
A-1180 Vienna (AT)

(74) Representative: **Wibbelmann, Jobst, Dr., Dipl.-Chem. et al**
Wuesthoff & Wuesthoff,
Patent- und Rechtsanwälte,
Schweigerstrasse 2
81541 München (DE)

(56) References cited:
US-A- 4 970 200

发明专利证书

证书号　　第 74558 号

发明名称：稳定、可食、易吸收的NADH和NADPH治疗组合物

发明人：乔格·G·D·伯克迈耶

专利号：ZL 94 1 91939.0　国际专利主分类号：A61K　9/36

专利申请日：1994 年 3 月 25 日

专利权人：美国伯克迈耶

授权公告日：2001 年 10 月 10 日

本发明经过本局依照中华人民共和国专利法进行审查，决定授予专利权，颁发本证书并在专利登记簿上予以登记。专利权自授权公告之日起生效。

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专利号

局长 王景川

二〇〇一年十〇月十〇日

特　許　証

特許第２５３３７０９号

平成０３年　特　許　願第３４５７６６号

発明の名称　　体力増強剤

特許権者　　オーストリア国　１０９０　ヴィエン　シュヴァルツシュパニエルシュトラーセ　１５
国籍　オーストリア国
ユルク　ビルクマイヤー

発　明　者　　ユルク　ビルクマイヤー
ヴァルター　ビルクマイヤー

この発明は、特許するものと確定し、特許原簿に登録されたことを証する。

平成　８年　６月２７日

特　許　庁　長　官　　清　川　佑　二

ENADA®

is marketed as a

nutritional supplement

The Original New Packaging Design

ENADA® NADH

has been marketed as a

nutrional supplement

in the U.S.

since 1995

What is Aging ?

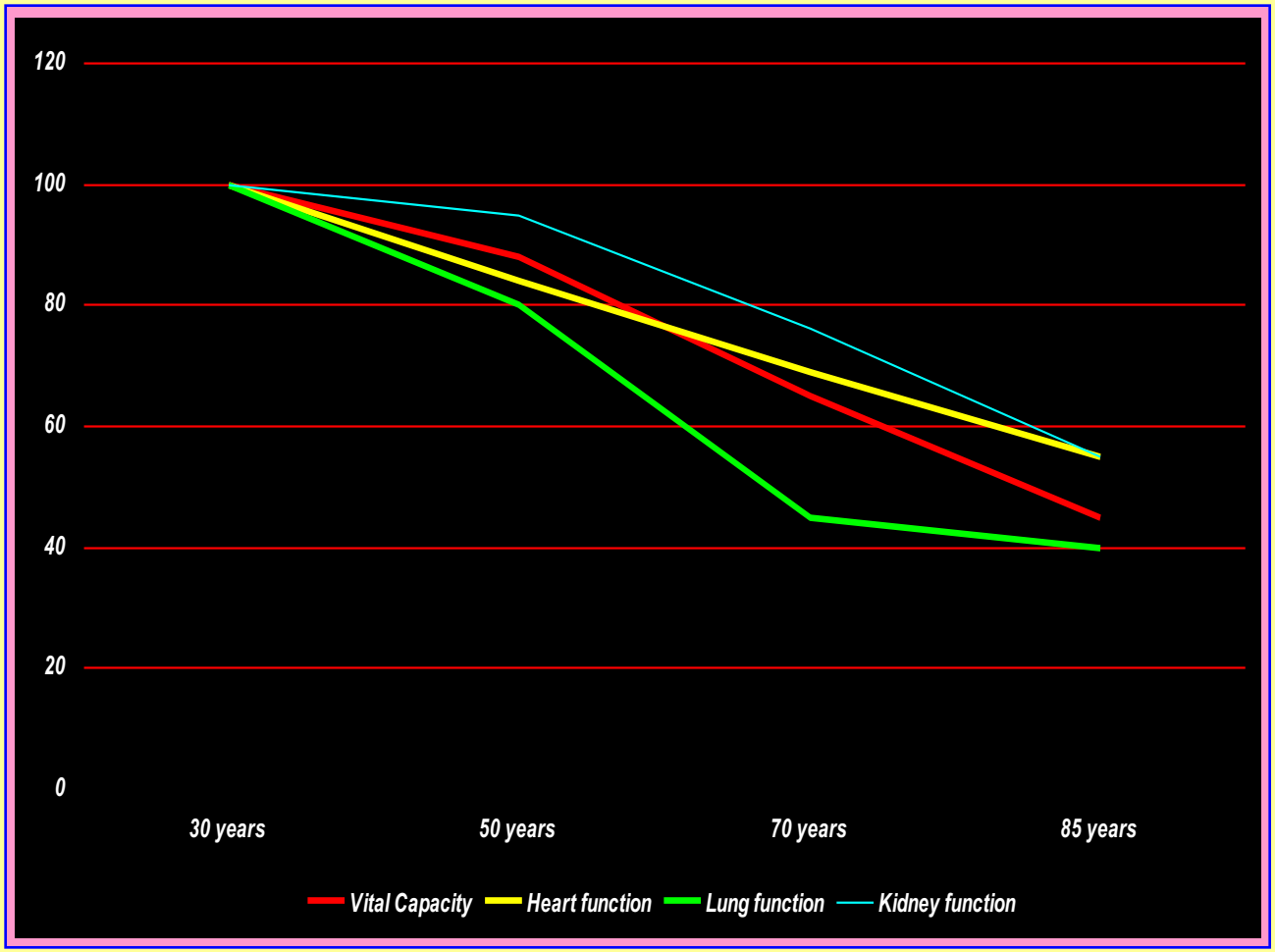
- Aging at the **organ** level
- Aging at the **cellular** level

Aging at the **organ** level

- **By limited blood (oxygen) supply**
- **by organ damaging substances:**
- Alcohol – Liver
- Smoking – Lung
- Blood pressure medication – Brain
- Cholesterol lowering drugs – Muscle
- Cytostatic drugs - Heart

Consequence: Improve blood circulation (by physical exercise) and avoid toxines and drugs

Decline of physiological functions with age



Aging at the **cellular** level

- **Energy production declines with aging of the cell**
- **If the energy production of the cell declines below a certain threshhold the cell will die**

Consequence: Keep **energy production** of the cell high

Why does energy production in a cell decline ?

Influences of factors

(a) Inside the cell

(b) Outside the cell

Intra-cellular factors : Oxidation, Free radicals, defect enzymes

Extra-cellular factors: Radiation, UV-Light and chemical Toxines

Metabolic and Energetic Changes During Apoptosis in Neural Cells

- J.C.Mills, D.Nelson, M.Erecinska and R. Pittman
- Journal of Neurochemistry (1995)
- These cells , upon exposure to stimuli that cause single-stranded DNA breaks, experience a large increase in poly (ADP-ribose) polymerase activity, which leads to depletion of cellular NADH
- **The loss of NADH is thought to lead to ATP depletion, which, in turn, leads to cells death.**

If a cell is already damaged
can we repair it
to full functionality ?

Yes,
we can by
ENADA

- **ENADA protects cells from damage by toxic agents such as doxorubicin and cisplatin used for chemotherapy of cancer**

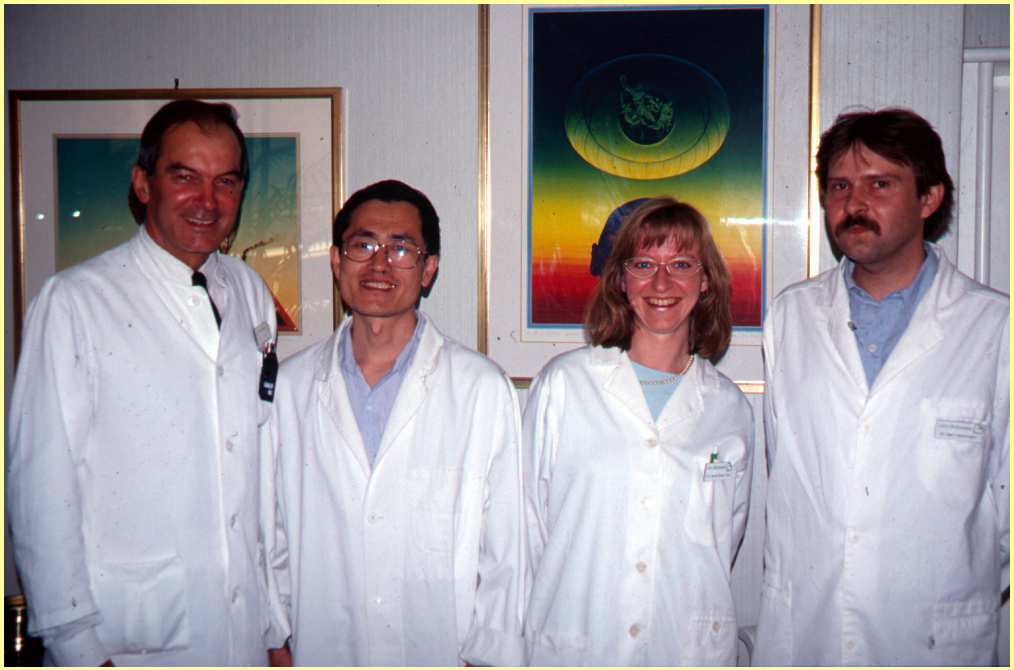
- **ENADA promotes cell damage repair. Altered or damaged cells can be repaired to gain full functionality.**

- Cisplatin, one of the most frequently used agent for cancer treatment causes damages of cells (cancerous as well as normal ones) by destructing the cell membrane, the mitochondria and the nucleus.
- Preincubation of the cells with **ENADA** prevents the severe sometimes fatal changes induces by Cisplatin.
- Already altered and damaged cells can be restored to full functionality by incubating the cells with **ENADA.**

The Reduced Coenzyme Nicotinamide Adenine Dinucleotide (NADH) repairs DNA damage of PC12 cells induced by doxorubicin

JR Zhang, K.Vreko,K.Nadlinger. D.Storga
GD.Birkmayer and G.Reibnegger

J.Tumor Marker Onco.13, 5-17 (1998)



G. Birkmayer J. Zhang D. Storga K. Nadlinger

J.Zhang , Professor of Clinical Oncology at the University of Guangzhou (Canton) in China, performed all the DNA repair studies

The Reduced Coenzyme Nicotinamide Adenine Dinucleotide (NADH) Prevents Hepatic Cells from Apoptosis by Mitochondria dependant signalling Pathway

Meng XU, Jiren Zhang

Int. Journal of Modern Cancer Therapy, 3, 38-41 (2000)

JOURNAL OF TUMOR MARKER ONCOLOGY
Volume 17, Number 4, Winter 2002
The International Academy of Tumor Marker Oncology Inc. Publishers

The Cytoprotection of Nicotinamide Adenine Dinucleotide (NADH) in the Mitochondria Regulation Mechanism*

Xu Meng, Zhang Jiren[1], Sarah SC Hui[2]

Department of Oncology, Nan Fang Hospital, The First Military Medical University, Guangzhou 510515, [1]Department of Oncology, Zhu Jiang hospital, [2]School of Traditional Chinese Medicine, The University of Hong Kong, Hong Kong SAR, P.R. China

*The study was supported by a grant from SPACE of the University of Hong Kong

NADH is an essential component of enzymes for many metabolic reactions and energy production in cell. Mitochondria are well known to have a critical function in energy metabolism and damage to mitochondria has been related to apoptosis. Cytoprotection of NADH in apoptotic damage induced by Cisplatin (DDP) was explored to clarify the mechanism of mitochondria regulation pathway. Laser scanning confocal microscope was employed to detect mitochondria membrane potential $\Delta\psi m$ with fluorescent probe R123, intracellular free Ca^{2+} value with probe Flu-3-AM, pH value with probe SNARF-1-AM and reduced oxygen species (ROS) value with probe H_2DCF in hepatocytes. The expression of cytochrome c and poly (ADP-ribose) polymerase (PARP) protein was detected by Western blot. Mitochondrial oxidative phosphorylation was measured polarographically by determining oxygen consumption rate state 3 and state 4, respiratory control rate (RCR) and ADP/O ratio. Compared with the group of control, in the group of DDP the fluorescence intensity of R123, Fluo-3/AM, SNARF-1-AM and H_2DCF was raised obviously, which indicated that the reduction of mitochondria membrane potential, the improvement of intracellular Ca^{2+} and ROS value was kept. In the group of control, the expression of cytochrome c was released from mitochondria matrix to cytoplasm in the group of DDP and cytochrome c was not released in the group of NADH/DDP. 113 kDa PARP was detected in the group of control, but in the group of DDP PARP was broken into 89 kDa fragment. PARP kept integrated in the group of NADH/DDP. Compared with the group of control, the value of S_3, RCR and ADP/O reduced more than 38%, 35% and 40% in the group of DDP. There was a significant difference between the group of NADH/DDP and DDP. The change of S_3 and mitochondria RCR reduction resulted in hepatocyte injury induced by DDP. NADH could prevent DDP-induced mitochondria impairment. Improving mitochondrial function represents a novel therapeutic strategy in cytoprotection of chemotherapy.

ISSN 1007-9327 CN 14-1219/R World J Gastroenterol 2003 Aug;9(8):1781-1785

X-ray induced L02 cells damage rescued by new anti-oxidant NADH

Fa-Quan Liu, Ji-Ren Zhang

Fa-Quan Liu, Ji-Ren Zhang, Department of Oncology, Zhujiang Hospital, First Military Medical University, Guangzhou 510282, Guangdong Province, China
Supported by Healthcare Research Fundation of the Tenth Five-Year Plan of PLA, No, 01MA138
Correspondence to: Fa-Quan Liu, Department of Oncology, Zhujiang Hospital,First Military Medical University, Guangzhou, 510282, China. liufaquan@163.net
Telephone: +86-20-85143202 Fax: +86-20-85143200
Received: 2002-08-06 Accepted: 2002-10-18

Abstract

AIM: To explore molecular mechanism of nicotinamide adenine dinucleotide (NADH) antagonization against X-ray induced L02 cells damage.

METHODS: L02 liver cells were cultured in RPMI 1640, exposed to X-ray irradiation and continued to culture in the presence or absence of NADH. Cellular viability was analyzed by routine MTT methods. The percent age of apoptotic cells and positive expressions of p53, bax and bcl-2, fas, fasL proteins were determined by FCM. Level of intracellular ROS was determined by confocal microscope scanning. Morphological change was detected by scanning electron micrograph.

RESULTS: The viability of L02 cells was decreased with increasing dose of X-ray irradiation. NADH could not only eliminate the apoptosis induced by X-ray irradiation, but also up-regulate expression of bcl-2 protein and down-regulate expression of p53, bax, fas and fasL proteins ($P<0.05$). At the same time, NADH could reduce level of intracellular ROS in radiated L02 cells.

CONCLUSION: NADH has marked anti-radiation effect, its mechanism may be associated with up-regulation of bcl-2 expression and down-regulation of p53, bax fas and fasL expression, as well as decline of intracellular ROS. However, further investigation of its mechanism is worthwhile.

Liu FQ, Zhang JR. X-ray induced L02 cells damage rescued by new anti-oxidant NADH. World J Gastroenterol 2003; 9(8): 1781-1785
http://www.wjgnet.com/1007-9327/9/1781.asp

What is Anti-Aging ?

- Repair of damaged cells and tissues
- Increase of energy production in a cell
- Extend life-span of cells, tissues and organs

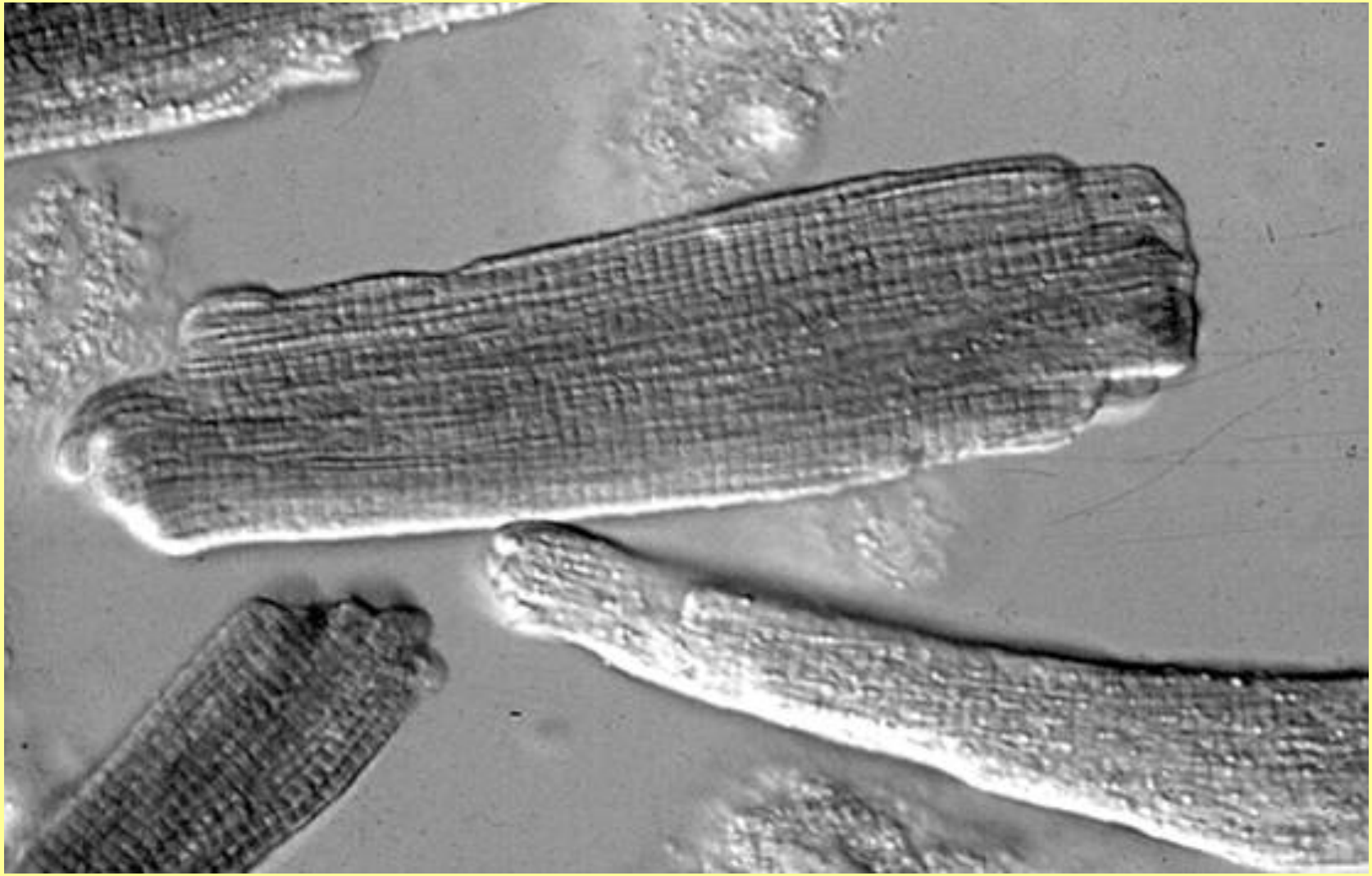
Can we increase the energy production in a cell ?

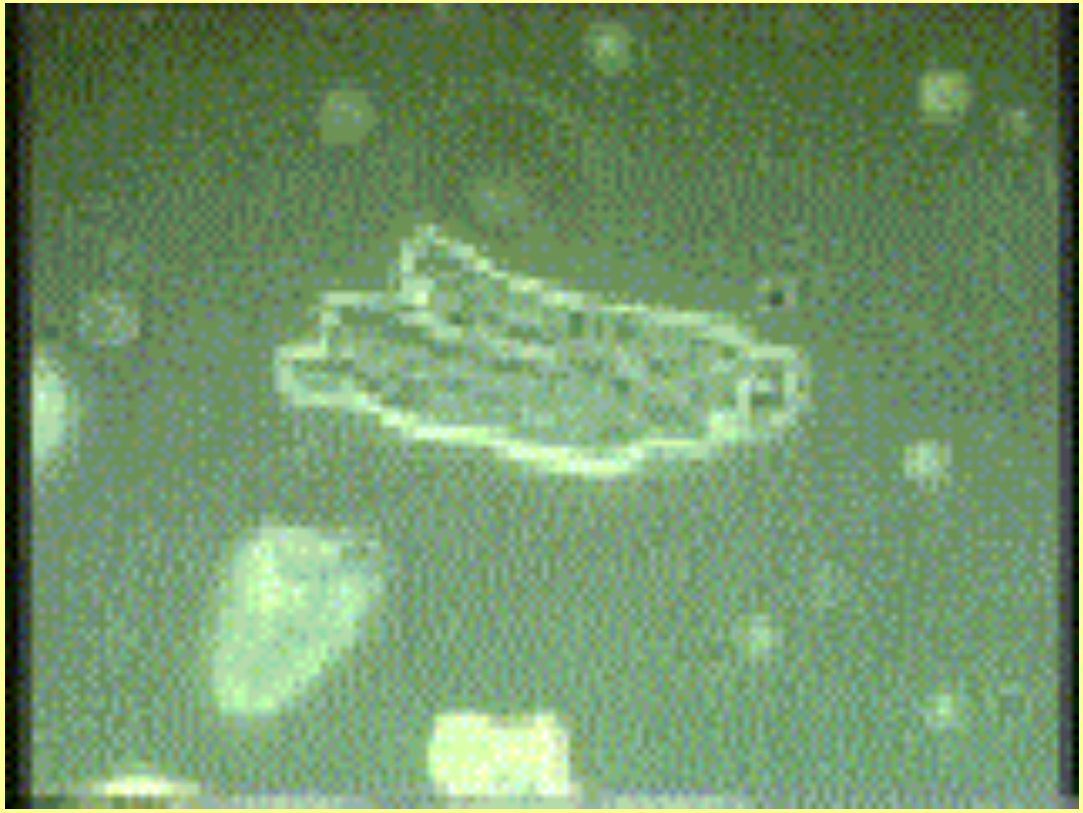
Yes,

we can by

ENADA

Microscopic Picture of isolated heart cells





ATP is the abbreviation for **A**denosin-**T**ri-**P**hosphate

ATP is a substance with a
high energy content in the molecule.

ATP is used by the cell for all
energy - consuming production processes

When isolated heart cells are incubated with ENADA (ENADA is outside the cell) , the **ATP** concentration inside the heart cells **increases.**

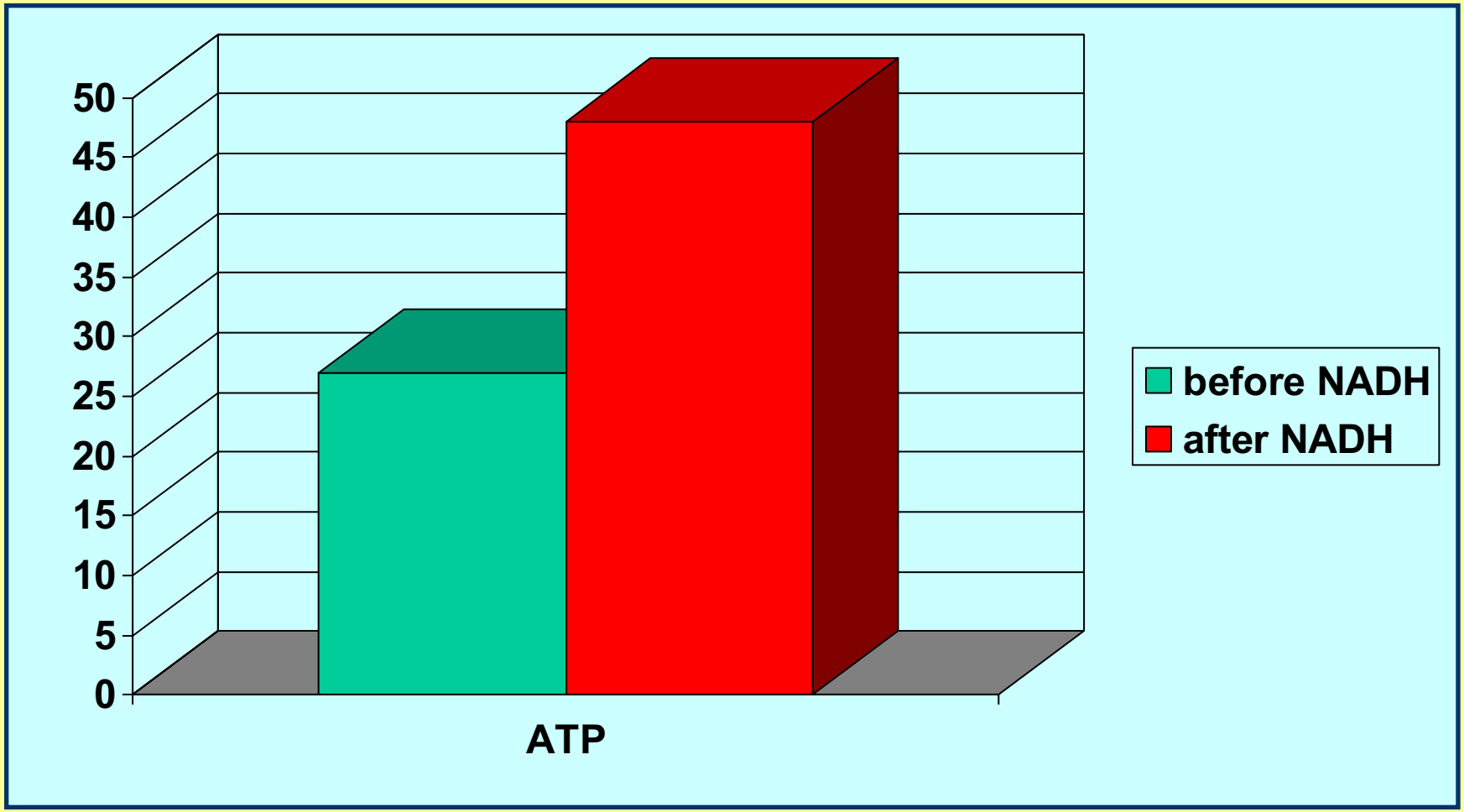
In other words, these heart cells do have more **ATP- energy.**

Hence, they can function better and can **live longer.**

A T P concentration of heart cells

before (green bar) & after (red bar) incubation

with **ENADA NADH**

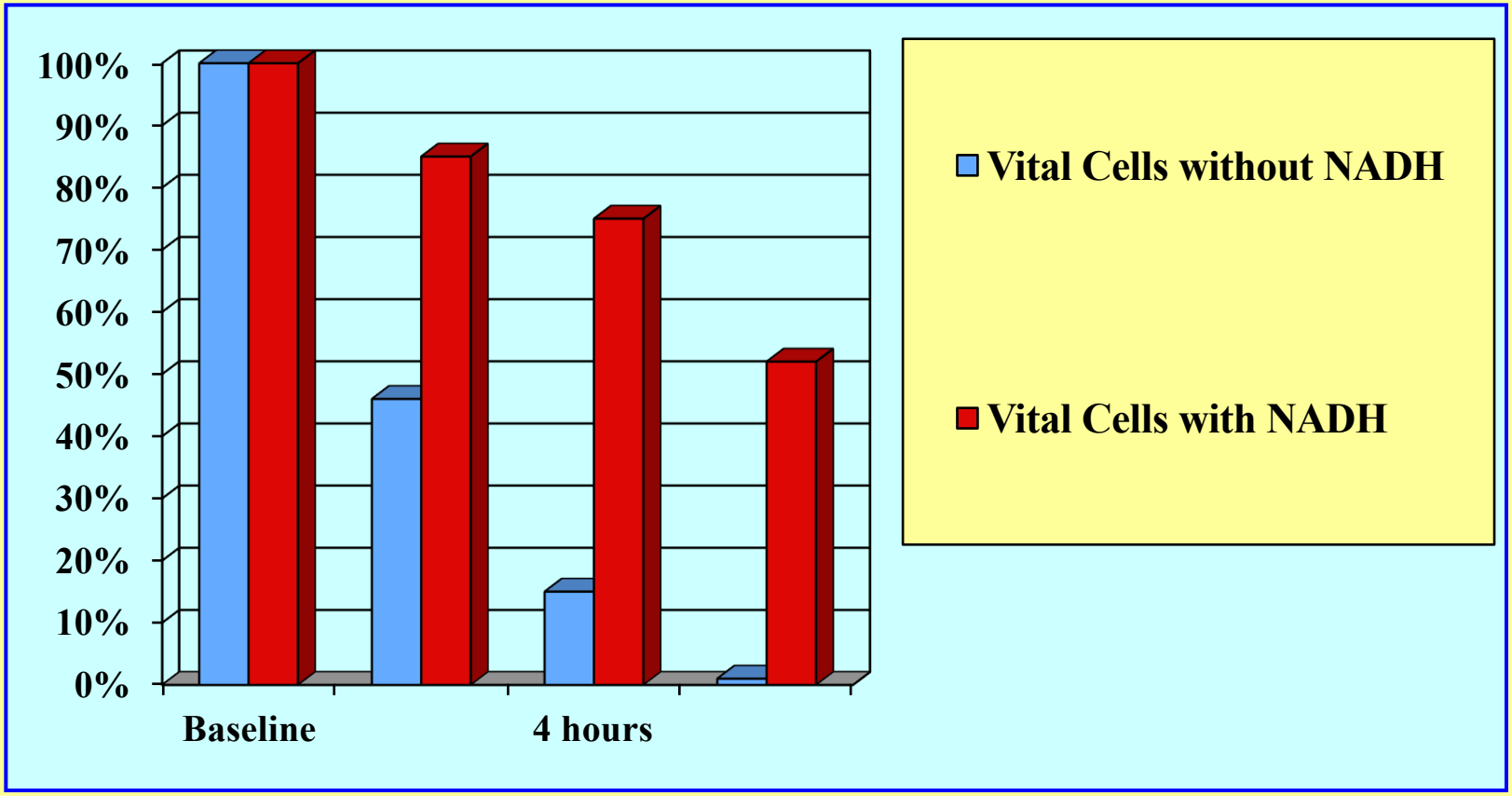


ENADA N A D H-supplementation decreases pinacidil-primed $I_{K(ATP)}$ in ventricular cardiomyocytes by increasing intracellular ATP

Pelzmann B, Hallström S, Schaffer P, Lang P,Nadlinger K, Birkmayer GD, Vrecko C, Reibnegger G and Koidl B

. **Brit. J. Pharm. 2003 139, 749-754**

Vitality of heart cells with and without ENADA NADH



Heart cells in the presence of ENADA NADH

This sensational new discovery has enormous implications for protection of the heart and other organs.

If cells live longer, all organs and the entire organism live longer.

In other words, **ENADA**

has a - scientifically documented - **anti-aging effect.**

KENYON & KENYON
Intellectual Property Law

Richard M. Rosati
Direct 212.908.6472
rrosati@kenyon.com

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New York, NY 10004-1050
212.425.7200
Fax 212.425.5288

February 3, 2003

VIA DHL COURIER

Dr. George D. Birkmayer
Labor Birkmayer & Medinfo Ltd.
Schwarzpanierstrasse 15
A-1090 Viena, Austria

Re: New U.S. Patent Application
METHOD OF PROLONGING THE LIFE-SPAN OF
LIVING CELLS USING NADH, NADPH AND ADP-RIBOSE
Our Ref. 1642/58

Dear George:

We wish to advise you that the above-identified application was filed on December 27, 2002 under Serial No. 10/330,973.

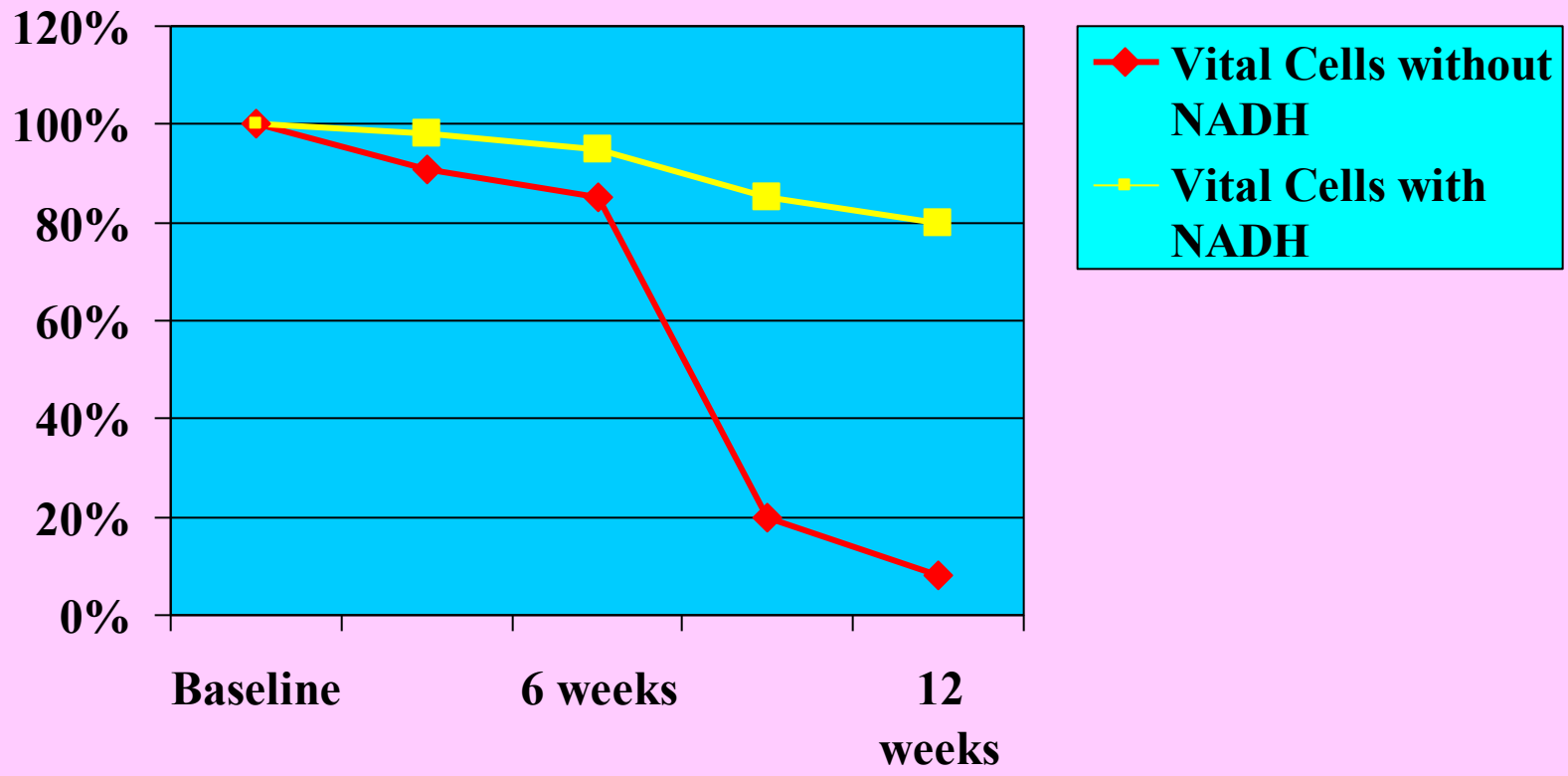
What about other human cells ?

Can their life-span be extended by **ENADA** ?

Yes,

it can

Vitality of red blood cells with and without ENADA NADH



Red blood cells in the presence of ENADA NADH live much longer / with vitality and can be kept much longer for

Extension of the expiring date of blood donations by NADH

Blood for transfusion can only be stored for 6 weeks by law

In the R&D department of Birkmayer Laboratories it was discovered , that blood can be kept 12 weeks or even longer by addition of ENADA NADH

Economic implication of this findings:

1. The Austrian Red Cross sells 5 million blood bags per year for 300 million Dollars

2. One third of the blood bags have to be discarded because of the expiring date of 6 weeks.

3. If the Red Cross can use only 50% of the discarded blood it can make additional 50 (fifty) million Dollars only in Austria.

ENADA® NADH
boosts cellular ATP energy also in human subjects

Can we measure the increase ATP energy by **ENADA® NADH** in human subjects ?

Yes , we can by a new blood test developed in our laboratory

Prof. **Birkmayer**
Health Products

E N M A®

A - patented - new blood test for the determination of the energy status

Developed by Birkmayer Laboratories, Vienna, Austria
www.birkmayer.com

What is the **ENMA** Test ?

E xtracellular

N A D H

M etabolization

A ssay

How does the **ENMA** test work?

The **ENMA** test measures
how much *N.A.D.H.*
is metabolized
by blood cells.

The **N.A.D.H.** metabolization rate of blood cells is indirectly related to the ATP (energy) content of blood cells.[1)]

1) Nadlinger et al. Biochim. Biophys.Acta 1573: 177-182 (2002)

Hence if blood cells have a low ATP (energy) content

they metabolize a lot of

N.A.D.H.

ELSEVIER

Biochimica et Biophysica Acta 1573 (2002) 177–182

BIOCHIMICA ET BIOPHYSICA ACTA
BBA

www.bba-direct.com

Extracellular metabolisation of NADH by blood cells correlates with intracellular ATP levels

Karl Nadlinger *, Wilhelm Westerthaler, Danijela Storga-Tomic, Jörg G.D. Birkmayer

Department of Research and Development, Birkmayer Laboratories, Schwarzspanierstr. 15, A-1090 Vienna, Austria

Received 26 April 2002; received in revised form 20 August 2002; accepted 4 September 2002

Abstract

A new assay allowing quantitation of extracellular NADH metabolisation by intact blood cells was compared with the intracellular ATP/ADP ratio of these cells. The sensitivity, reproducibility and NADH specificity of this assay were determined. The diagnostic potential of this test was examined in a study with highly conditioned athletes. NADH consumption was measured before and immediately after maximum aerobic performance as well as 1 day later and was compared with the ATP/ADP level in these blood cells. A significant decline of cellular energy after aerobic performance was detected with both approaches to a similar extent ($P<0.01$). However, the extracellular NADH metabolisation assay (ENMA) is more convenient to perform than the determination of intracellular ATP/ADP. Due to its easy and versatile handling, a huge array of possible applications like monitoring the training efficiency of athletes, the fitness of senior citizens or the recovery from disease may be envisioned.

Keywords: NADH; ATP; Blood test; Sports

The **ENMA** test
has received
world wide patents

US006383771B1

(12) **United States Patent**
Birkmayer

(10) **Patent No.: US 6,383,771 B1**
(45) **Date of Patent: May 7, 2002**

(54) **ENZYME-BASED ASSAY FOR DETERMINING EFFECTS OF EXOGENOUS AND ENDOGENOUS FACTORS ON CELLULAR ENERGY**

(75) Inventor: **Georg D. Birkmayer**, Vienna (AT)

(73) Assignee: **Birkmayer Pharmaceuticals**, New York, NY (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 76 days.

(21) Appl. No.: **09/631,692**

(22) Filed: **Aug. 3, 2000**

Related U.S. Application Data

Reichmann, et al., Respiratory Chain and Mitochondrial Deoxyribonucleic Acid in Blood Cells from Patients with Focal and Generalized Dystonia, Movement Disorders, 1994, 9(6), 597–600.

Mitzkat, et al., Enzyme Patterns of the Energy–Linked Metabolism in Blood Cells of Human Diabetics, Hormone and Metabolic Research, 1972, 4(2), 107–110.

Ramakrishna, et al., Influence of Cerebral Ischemia and Post–Ischemic Reperfusion on Mitochondrial Oxidative Phosphorylation, J. Bioenerg. Biomembr., 1990, 22(1), 61–80.

Primary Examiner—Jean C. Witz
(74) *Attorney, Agent, or Firm*—Kenyon & Kenyon

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) **EP 0 911 417 B1**

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention of the grant of the patent:
28.08.2002 Bulletin 2002/35

(51) Int Cl.[7]: **C12Q 1/26**, C12Q 1/32, C12Q 1/25

(21) Application number: **98119764.3**

(22) Date of filing: **22.10.1998**

(54) **Enzyme-based assay for determining effects of exogenous and endogenous factors on cellular energy production**

Auf Enzym-gegründetes Assay zur Bestimmung der Wirkung von exogenen und endogenen Faktoren auf Zellenergie-Bildung

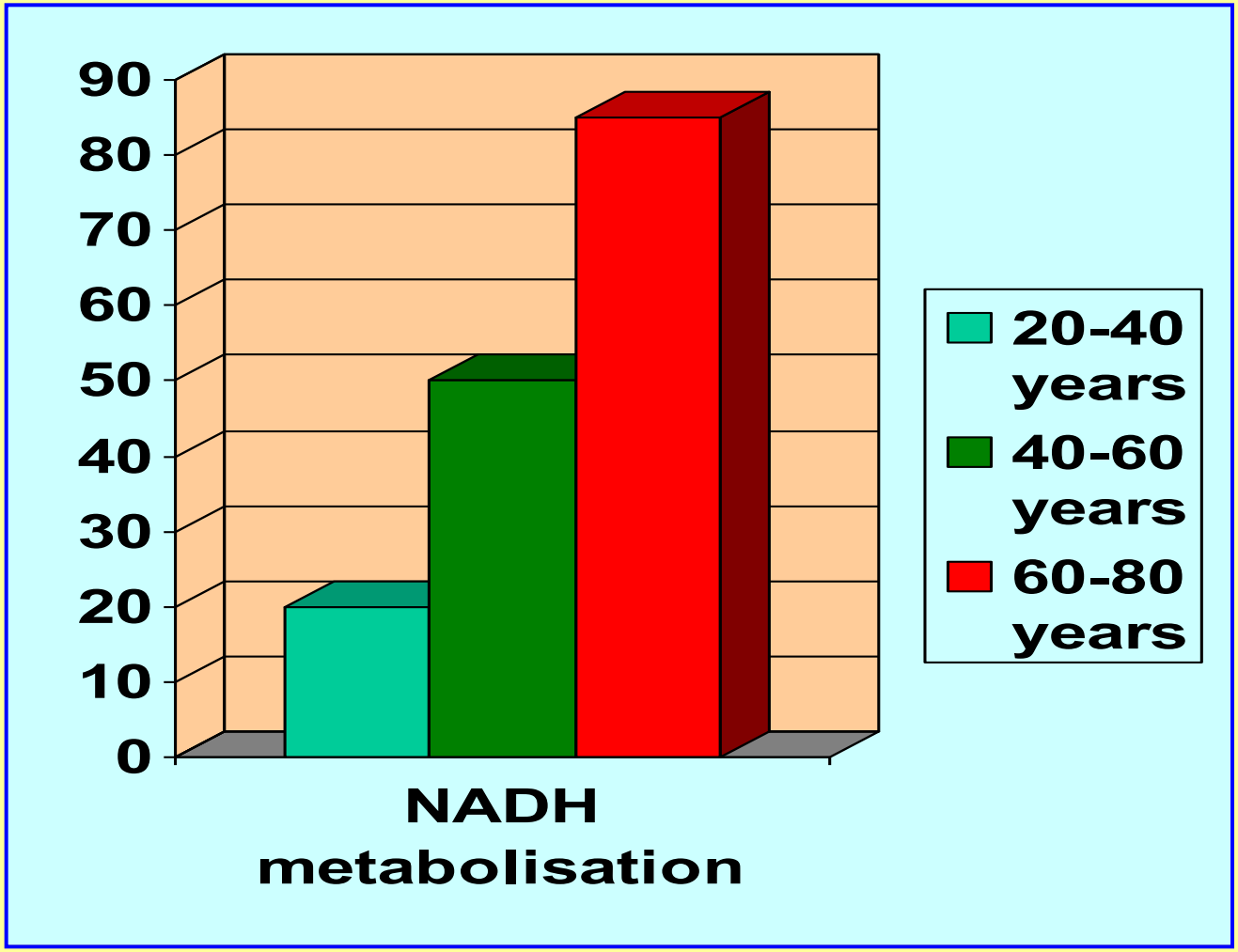
Test enzymatique pour déterminer les effets d'agents exogènes et endogènes sur la production d'énergie cellulaire

The **ENMA** test
was developed
to measure the
effect of
„energy increasing“
substances
in particular
that of
ENADA – N.A.D.H.

People with a high energy level (athletes), need less NADH

People with a low energy level (old or sick people), need a lot of NADH

NADH metabolization of blood from people with increasing age

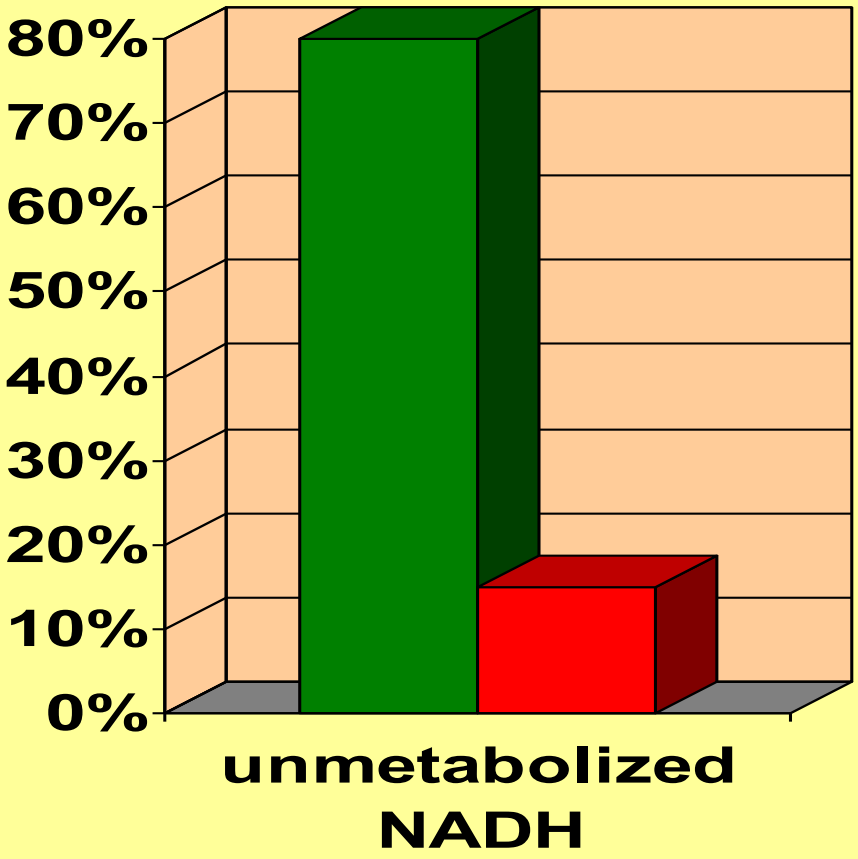


Older people metabolize much more NADH as they need more ATP energy

Marathonrunners **before** the race have a high energy level, hence they metabolize **little** **N.A.D.H.**

Marathonrunners **after** the race have a low energy level, hence they metabolize **much** **N.A.D.H.**

NADH – metabolization by blood from marathon runners



- **The NADH which is not metabolized reflects the ATP content (energy-level) of the blood cells.**

Before the start the blood of the runners metabolizes only 20% of the NADH added, because the runners have enough ATP (energy) .

After the run the blood metabolizes 85% of the NADH added, because the ATP (energy) was used up during the marathon run.

On the effect of **ENADA – N.A.D.H.** with marathon runners

- Double blind placebo controlled cross-over study
- Group-1 were taking **ENADA –N.A.D.H.** 30 mg per day for 4 weeks
- Group-2 were taking Placebo pills

- The **ENMA** test was performed before start, after the run and 24 hours after the run.

On the effect of *ENADA – N.A.D.H.* with marathon runners

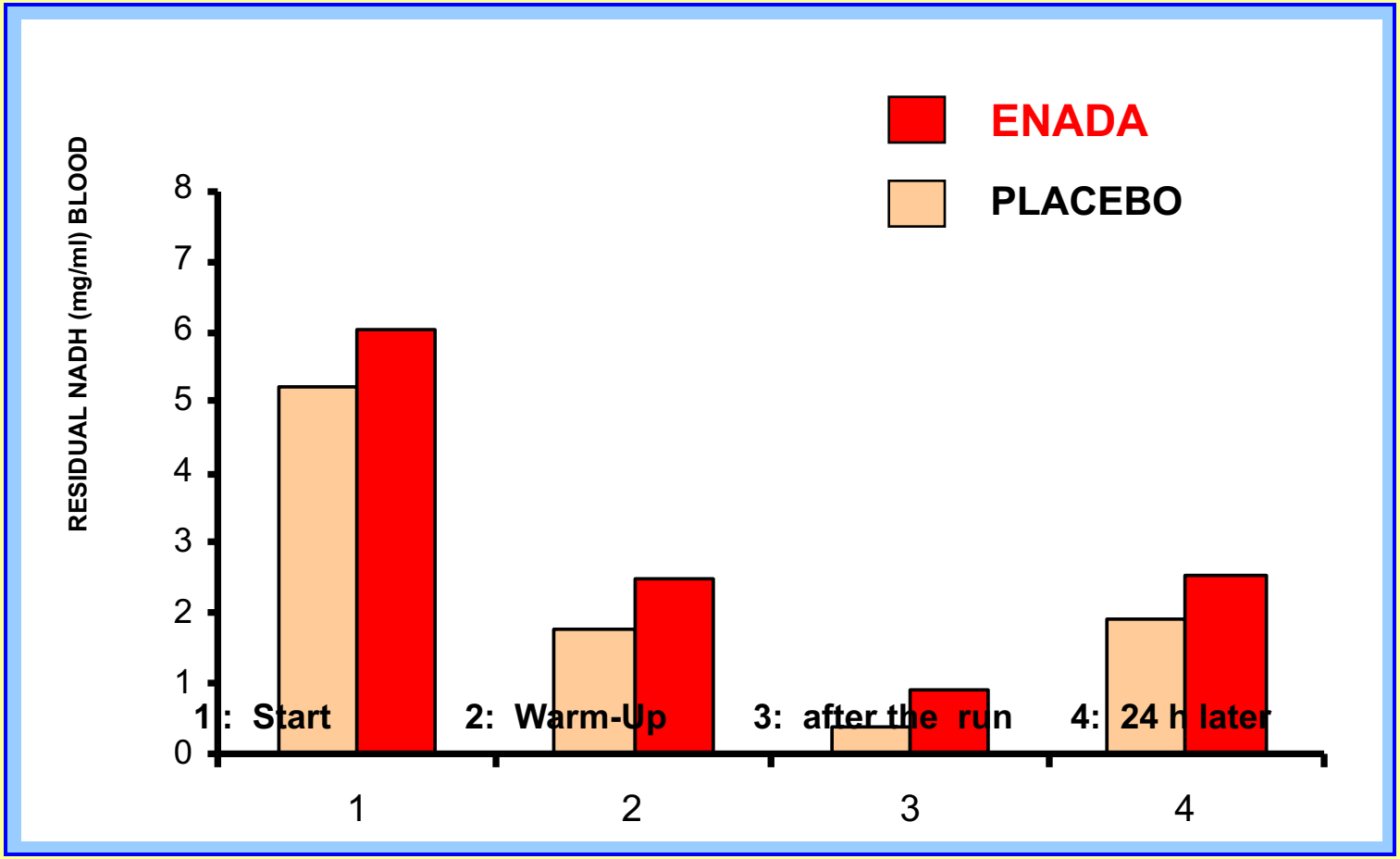
Results:

- The runners had a low NADH metabolization rate (= high ATP-energy level) before the race and a high NADH metabolization rate (=low ATP-energy level) after the marathon run.

  The runners taking *ENADA* had a lower NADH metabolization rate (=higher ATP-energy level) than the runners taking the placebo pills.

- These results provide scientific proof that *ENADA-N.A.D.H.* increases cellular energy.

ENMA - test with marathon runners after intake of **ENADA – N.A.D.H.**



Applications of the **ENMA** test (1)

- Testing of energy enhancing substances
- Testing of „energy drinks“
- Testing of anabolic substances
- Controlling the training of athletes
- Controlling the energy level of elderly

Applications of the **ENMA** test (2)

- Testing the energy level of sick people
- Testing the energy level before and after medical treatment (surgery, radiation, chemotherapy etc.)
- Testing of energy level after rehabilitation (coronary heart disease, lung disease etc.)

ENADA® - NADH

and

Athletic performance

ENADA® - NADH
and
Athletic performance

7 % more muscular energy

Higher oxygen supply for the muscle

Lower lactate levels

Better performance on spiroergometry

ENADA® - NADH

and

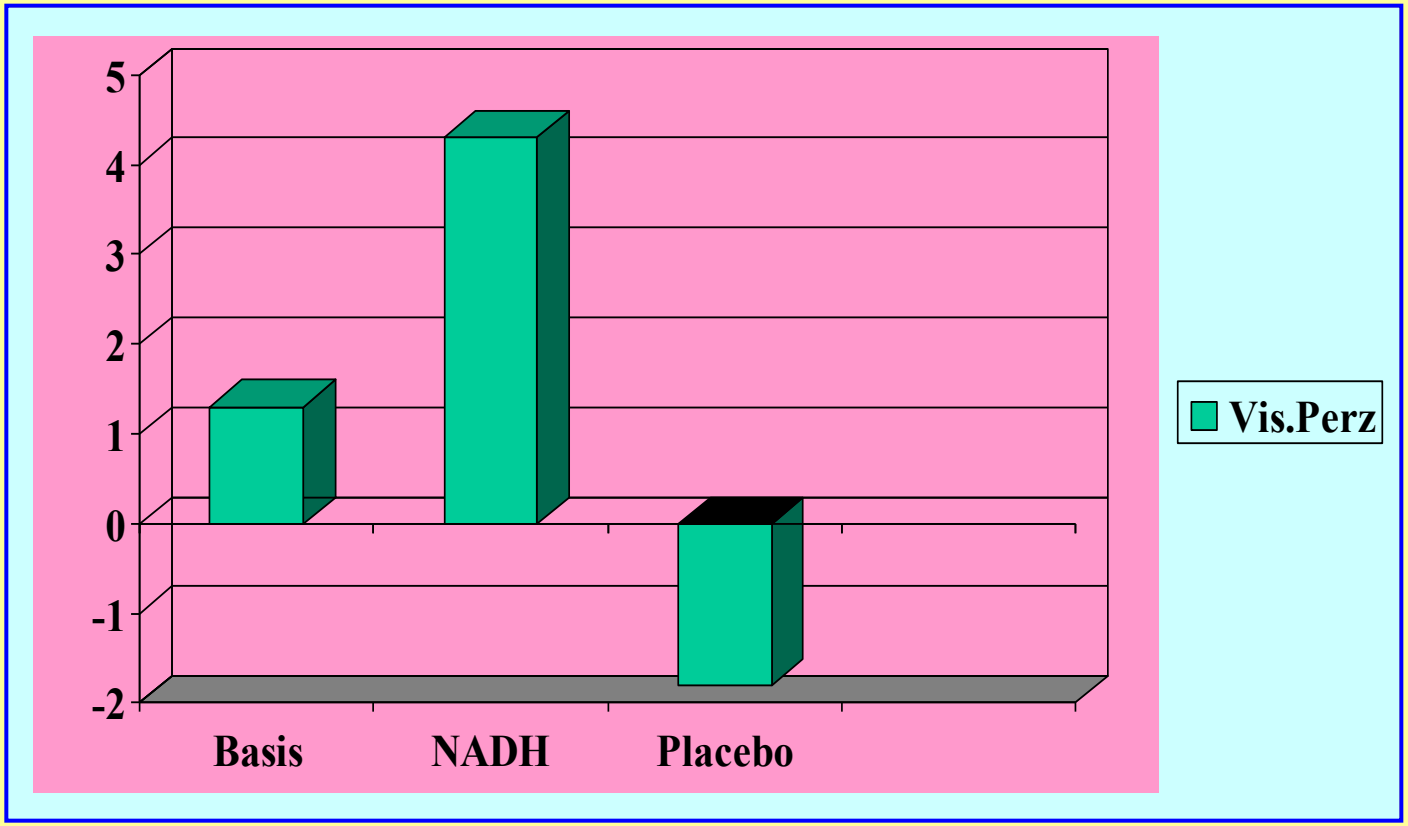
Cognitive performance

Study shows:
NADH alleviates symptoms of cognitive impairment caused by sleep deprivation

- Where was the study performed:
  2001 at Cornell University New York, Publication in print

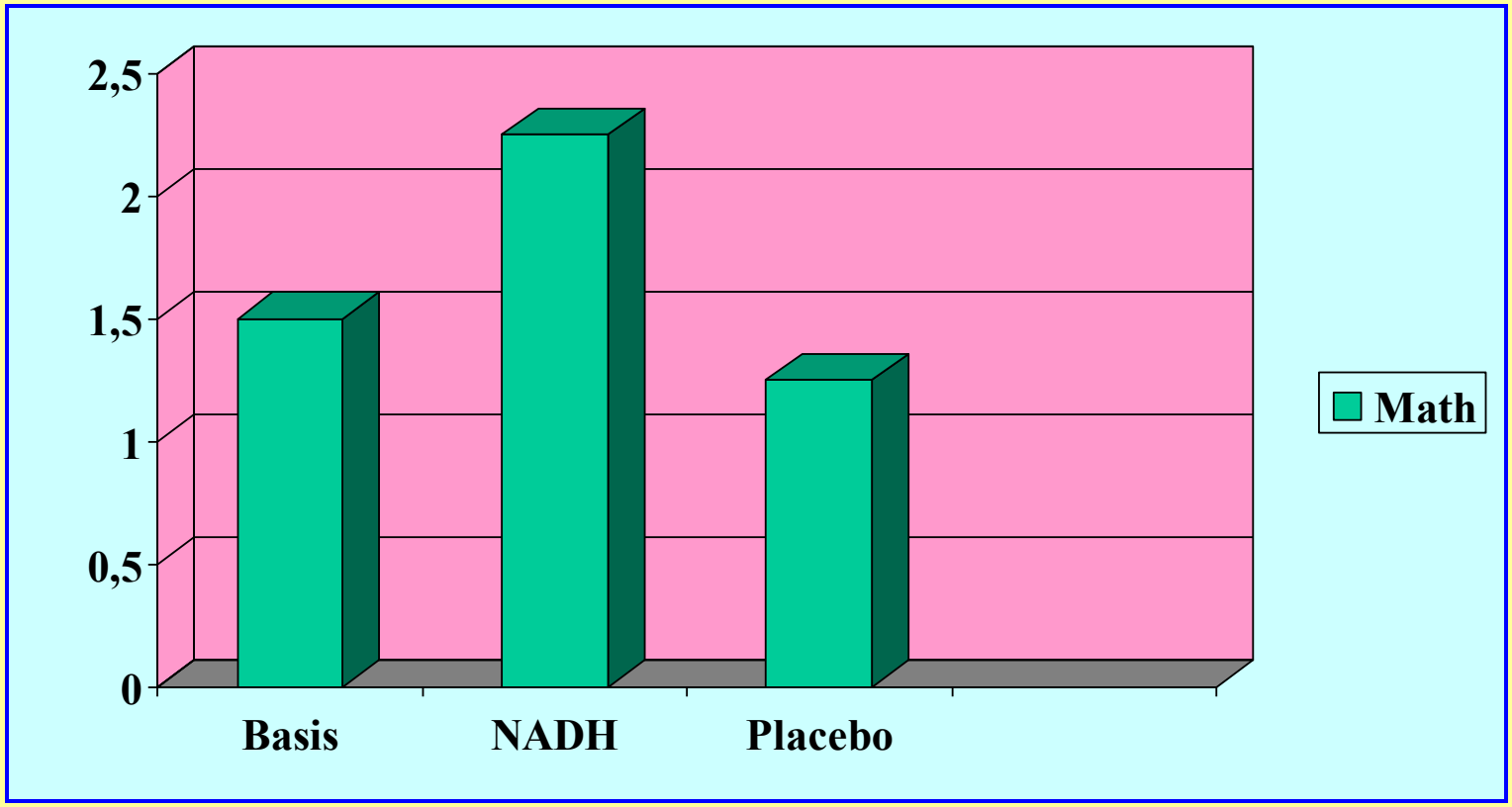
- How: Double-blind, placebo controlled study with middle-aged healthy individuals:
  - Subjects were kept awake one day and one night (24 hrs) ; one group took placebo in the morning after 24 hours of sleep deprivation,
  - the other group *ENADAlert* (quick acting NADH)
  - At day 1 in the morning and on the next day in the morning (after 24 h sleep deprivation) tests for visual perception mathematical problem solving capability and reaction time.

Visual Sequence Comparison Performance as measured by Cog-Screen®



The performance with NADH (after 24 hrs <u>without</u> sleep) was 3 points better than at base line (after a <u>full night sleep</u>)

Mathematical problem solving skills as measured by Cog-Screen®



The performance with NADH (after 24 hrs <u>without</u> sleep) was 0.7 points better than at base-line (after a <u>full night sleep</u>

The Sensational Results

The subjects taking
ENADA - NADH
showed higher alertness
faster reaction-time and
better visual perception
after 24 h of sleep deprivation than
the day before
after a full night sleep.

After a press conference by Cornell University reports of these sensational results were shown by :

ABC: „Good morning America“
CNN, Fox News

Reports were printed also in:
„NEWSWEEK“
„Wall Street Journal“

Weill Cornell Westchester
21 Bloomingdale Road • White Plains NY, 10605

Effectiveness of NADH in Alleviating Effects of Sleep Deprivation in Healthy Middle-Aged Adults*

Moline ML, Rebeta JL, Flye BL, Zendell SM, Broch L, Ford T, Zak R, Kay GG (2)

(1) Sleep-Wake Disorders Center, Department of Psychiatry, New York Presbyterian Hospital-Weill Medical College of Cornell University
(2) Department of Neurology, Georgetown University School of Medicine

Psychiatry

STUDY ABSTRACT

Aims: Sleep deprivation affects cognitive performance and quality of life. It impacts otherwise healthy individuals who cross time zones, work shifts, or have certain sleep, psychiatric, or medical disorders. Despite manufacturers' claims, few over-the-counter substances have been shown in rigorously designed studies to improve daytime alertness following sleep deprivation.

We tested the ability of oral stabilized NADH (ENADAlert®, a nutritional supplement) to improve alertness, mood, and performance on cognitive tasks in middle-aged subjects after one night of total sleep deprivation. NADH has been shown to increase subjective measures of energy in Chronic Fatigue Syndrome[1]. NADH has also been shown to reduce the effects of jet lag on cognitive performance and sleepiness[2].

Methods: A double blind, placebo-controlled, randomized crossover study involving 25 healthy men and women ages 40-59 was conducted. Subjects were screened for medical, psychiatric, and sleep disorders and then underwent baseline cognitive assessment using a computerized battery (described below). On the baseline test day, subjects consumed sublingual placebo and had electrodes placed to simulate experimental conditions. They returned for one night of enforced, polygraphically-monitored wakefulness followed by morning consumption of sublingual NADH (ENADAlert 20 mg) or placebo determined randomly. During the day, cognitive testing, mood assessment (Profile of Mood States), and assessment of subjective (Stanford and Epworth Sleepiness Scales) and objective sleepiness (Multiple Sleep Latency Test – 3 naps) were performed. The complete CogScreen-Aeromedical Edition (CogScreen-AE) computerized cognitive battery assessed attention, memory, and reaction time among other factors. CogScreen-AE subtests were analyzed by throughput (correct responses/minute), accuracy, and speed (median reaction time to correct responses). All variables with sufficient data were combined in summary measures; two were discarded.

Results: Cognitive performance as assessed by overall throughput was significantly better (p=.018) following NADH than after placebo, after adjusting for baseline performance. Analysis of individual cognitive tests revealed that math throughput

(over)


COMING UP
PATRIOTISM
3

Prof. **Birkmayer**
Health Products

The International Press Reports on ENADA -NADH

Enzyme fights fatigue – study

REUTERS

WASHINGTON — A nutritional supplement based on an energy-giving natural enzyme can help in some cases of chronic fatigue syndrome, researchers will report today.

A team at Georgetown University in Washington tested the supplement, Enada, and found it helped as many as 72% of patients with the baffling condition.

More than 500,000 Americans have been diagnosed with chronic fatigue syndrome, and an estimated 2 million people believe they have it.

In the Georgetown study, approved by the U.S. Food and Drug Administration, Dr. Joseph Bellanti and colleagues said they tested 26 patients in the equivalent of a Phase II safety and efficacy trial.

For four weeks, half the patients got Enada and half got placebos.

For the next month, both groups got nothing, then the groups were switched — and the volunteers who got Enada the first time got a placebo for the next four weeks, while the second group got the supplement.

Neither group knew which they were getting at the time, placebo or supplement.

Writing in the Annals of Allergy, Asthma and Immunology to be published today, Bellanti's team reports that 31% of the patients said their symptoms got better while they took Enada, as opposed to 8% of those on placebo.

Then the researchers opened the trial, allowing all the volunteers to knowingly take Enada. After a year, 72% reported improvement.

Enada is the brand name of the company's version of a natural substance known as nicotinamide adenine dinucleotide, plus high-energy hydrogen (NADH).

It is a co-enzyme — the active part of the chemical reaction that enzymes produce in the body.

According to Menuco, the more NADH a cell has, the more energy it has.

The company hopes that can translate up to the level of a whole human being.

Unlike many supplement companies, Menuco went through some of the FDA protocols for testing. They were not required to.

In December, Hemispherx Biopharma Inc. applied for European Union approval of the first drug to treat chronic fatigue syndrome.

The drug, Ampligen, also is being tested for FDA approval. It consists of hydrocortisone, a synthetic version of one of the corticosteroid hormones produced by the adrenal gland.

Chronic fatigue syndrome is difficult to define, marked for the most part by an unexplained lack of energy.

Sometimes called myalgic encephalomyelitis, some doctors attribute it to psychological rather than physical causes.

Others say a virus, perhaps Epstein-Barr virus, may cause it, or perhaps an autoimmune disorder in which the body's immune system mistakenly turns against itself.

Daily News – Feb. 1999 USA


Newsweek

BEHIND THE WHEEL: Can a pill help his performance?

REMEDIES

Clearing the Mental Fog

A DOUBLE ESPRESSO CAN add spring to your step when you're short on sleep, but a compound called NADH may do more to sharpen your mind. NADH, which is sold over the counter under the trade names ENADA and ENADAlert, is not a stimulant and has no apparent side effects. It's a "co-enzyme" that, when produced naturally within the body, helps cells function more efficiently. Past studies have found that NADH supplements can help ease symptoms of jet lag and chronic fatigue syndrome. Now researchers are reporting that these same supplements can improve mental performance in people suffering from run-of-the-mill short-term sleep deprivation.

The new findings come from New York Presbyterian Hospital-Weill Medical College, where scientists enlisted 35 healthy, middle-aged volunteers to pull all-nighters in a sleep lab. After staying up for 24 hours, each volunteer received either a placebo or 20mg of NADH in sublingual (under-the-tongue) tablets. The pills had no effect on how tired people felt, but those taking the actual supplement gained an edge on cognitive tests. When asked to distinguish among patterns on a screen or to solve simple math problems, the subjects who got NADH performed more efficiently—generating more correct responses per minute—than those who got the placebo. On some exercises, several of the participants taking NADH performed better than they had in a normal, rested state.

Results from a 25-person trial are no cause for a run on this stuff, but the new findings suggest there is hope for us all. Nearly a third of U.S. adults manage less than seven hours' sleep each night, according to the National Sleep Foundation, and some 60 percent complain of frequent sleep problems. Delis and vitamin stores peddle countless remedies for fatigue, but few have undergone rigorous testing. If NADH works as well as the early results suggest, it could someday rival coffee as the foundation of a good breakfast.

GEOFFREY COWLEY

Newsweek December 17, 2001, Page 10. © 2001 Newsweek, Inc.

Newsweek – Dec. 2001 USA

Wiener Medizinische Wochenzeitschrift – 2002 AU


STUDIES CLARIFY BENEFITS FOR ATHLETES

Early studies found that NADH supplementation can ease the symptoms of brain fog and physical dysfunction found in patients suffering from chronic fatigue syndrome, Alzheimer's and Parkinson's disease. Recent research suggests that these same supplements can improve physical and mental performance in healthy people as well. In addition, no negative side effects have been reported.

In a study conducted at the New York Weill Cornell Medical Center, a group of 25 healthy volunteers were kept awake overnight and then given a series of mental tests the following day. These tests measured the speed and accuracy with which volunteers were able to think and solve problems under two separate conditions — after taking 20 mg of NADH and after taking placebo. "When the subjects took NADH, they performed more efficiently without experiencing any negative side effects," reports Margaret Moline, PhD, the lead researcher of the study. In some cases, participants who took the NADH actually performed better than they had in a fully rested state.

Other research has shown that NADH enhances reaction times and performance quality of competitive athletes. In a study that was conducted at the University of Freiberg, endurance athletes who were put on 30 mg of NADH daily for four weeks (10 mg three times per day) saw an average 7% increase in muscular energy vs. those given placebo. The subjects taking the NADH supplements also experienced increased efficiency in the body's utilization of oxygen.

"These results are unheard of when compared to any other supplement for the purpose of increasing energy and aerobic economy," says George Birkmayer, MD, PhD, the Austrian researcher who first recognized the therapeutic applications of NADH. "NADH can be characterized as the rocket fuel for the body. The more NADH a cell has available, the more energy it can produce."

If NADH is present in every living cell, why not rely on food sources for it? Because naturally occurring NADH, found primarily in red meat and poultry, disintegrates rapidly during cooking and digestion, says Joseph Bellanti, MD, a physician at the Georgetown University School of Medicine. People are particularly susceptible to depletions of NADH during periods of fatigue, stress, severe allergy or chronic infection, Bellanti explains.

NOT FOR CONTINUOUS USE

NADH doesn't make you hyper the way caffeine does, or give you the instant "up" of a candy bar where a half-hour later you find yourself coming down. Instead, you get a boost in physical energy and cognitive performance, especially beneficial before a workout or meeting.

Recommended daily dosages for NADH vary from 5 to 30 mg, depending on such individual factors as weight, metabolism and desired energy levels. NADH is available in a longer-acting form meant for ongoing use, as well as a quick-acting tablet that dissolves under the tongue and gives a shot of NADH to the body — a burst of energy that can be felt in as little as 20 minutes and lasts for three to five hours thereafter. According to Bellanti, his studies on patients with chronic fatigue syndrome indicate a cumulative increase in effectiveness after extended use of NADH.

But Ray Sahelian, MD, a physician who practices nutritional medicine in Marina Del Rey, Calif., and author of *Mind Boosters* (St. Martin's Press, 2000), doesn't think that taking NADH on a long-term daily basis is a good idea. According to him, uninterrupted use could create a tolerance level at which point the body might cease to benefit from the positive effects of NADH. "I wouldn't recommend it as part of an ongoing daily regimen, but I do feel very comfortable recommending it for occasional use," he says.

Most sources suggest using it daily for periods of up to four continuous months, then taking a month off. An alternative is to take it only two or three times a week, or on those occasions when you need that extra boost in energy.

Additional clinical trials in the United States and other countries are exploring the full potential of NADH for improved health and athletic performance. In the meantime, its top-notch safety record and proven effectiveness certainly make NADH a nutrient to check out.

Leelila Strogov, a graduate of the Massachusetts Institute of Technology, is a freelance writer who lives in Los Angeles.

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64 JUNE 2003 • physicalmag.com

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ScienceBackgrounder

NADH: Biological Rocket Fuel

By Georg D. Birkmayer, M.D., Ph.D.

All we need is energy. Every living cell needs energy to stay alive.

But exactly how is this energy for life produced? Hydrogen and oxygen react to form water and energy. The biological form of hydrogen is NADH, the abbreviation of nicotinamide-adenine-dinucleotide hydride. The oxygen comes from the air we breathe and is present in every living cell.

Rocket fuels are using the same principle. Hydrogen and oxygen in a liquid state react and cause an explosion which lifts the rocket from the ground. Hence, NADH can be regarded as biological rocket fuel with the sense difference that the energy is not wasted by an explosion but stored in chemical compounds such as ATP (adenosine triphosphate).

NADH was discovered in 1905 and found to be one of the most important coenzymes – hence its name coenzyme I.

How NADH Is Produced In Vivo

NADH consists of nicotinamide (also known as vitamin B3) and ADP (adenosine diphosphate). Nicotinamide is a precursor of NADH from which it is formed in the body when food is digested and degraded to sugar, amino acids and lipids. The hydrogen derived from the degradation of the substances is transferred to NADH in a metabolic pathway called citric acid cycle.

It is important to note that even high dosages of nicotinamide can not substitute for NADH. Vitamin B3 does not show any of the beneficial effects observed with NADH.

NADH is described extensively in all biochemistry textbooks. Unfortunately, it was used only for diagnostic purpose in blood tests. In the mid-1980s my late father and I did NADH for the first time therapeutically by administering intravenous infusions in Parkinsonian patients. The beneficial effect was remarkable: patients who were unable to get out of their seats could do so in an hour or two after IV application.

As a biological form of hydrogen, NADH is a very sensitive substance which reacts not only with oxygen but with many other chemical compounds even in state. Because of this, NADH was never considered for therapeutic application. After extensive year-long research we succeeded in developing a formulation in which NADH could be stabilized and made absorbable for the intestinal tract, and have received more than 50 worldwide patents. It is not only the composition but also the production process that renders NADH stable. Just blending NADH together with some fillers and excipients does not lead to a stable product; the substance will degrade rapidly in weeks.

Commercially available NADH is produced from yeast which is very rich in NAD (nicotinamidadenine-dinucleotide) the oxidized form of NADH. This NAD is reduced either chemically or biochemically to form NADH which is purified by several crystallization procedures. The final product contains

Reprinted From Supplement Industry Magazine, May 2001

Functions/Applications of NADH

NADH is the cofactor of more than 1300 enzymes in our bodies, however the most important biological functions that can be ascribed to this substance are:

- Cellular fuel for energy production;
- Key role in DNA repair and cell regeneration;
- Enhancer of the cellular immune system;
- One of the most potent antioxidants;
- Stimulator of dopamine, adrenaline and norepinephrine biosynthesis.

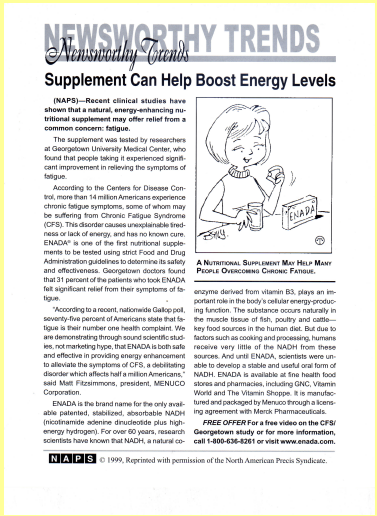
The more NADH a cell has available, the more energy it can produce. The heart and the brain are the organs that need the most energy. Hence, NADH shows the greatest benefit to these organs.

Studies at the University in Berlin have found that one particular brand of NADH is absorbed by the intestinal mucosa undegraded. It also reaches the brain by passing the blood brain barrier. After oral application of NADH we found an increase of the NADH in the brain cortex of rats. The more energy a cell produces the better it functions and the longer it can survive. This points to the enormous potential of NADH as cell protector and anti-aging potion.

Furthermore, NADH is essential for enzymes which do repair damaged DNA, rendering the tissue resistant to modifications which can lead to cancer and other degenerative diseases. The more NADH a cell has available, the better the body is protected from developing these types of diseases.

The cellular immune system also needs NADH for full func-

Supplement Industry Magazine – May 2001 USA


NEWSWORTHY TRENDS

Newsworthy Trends

Supplement Can Help Boost Energy Levels

(NAPS)—Recent clinical studies have shown that a natural, energy-enhancing nutritional supplement may offer relief from a common concern: fatigue.

The supplement was tested by researchers at Georgetown University Medical Center, who found that people taking it experienced significant improvement in relieving the symptoms of fatigue.

According to the Centers for Disease Control, more than 14 million Americans experience chronic fatigue symptoms, some of whom may be suffering from Chronic Fatigue Syndrome (CFS). This disorder causes unexplainable tiredness or lack of energy, and has no known cure. ENADA® is one of the first nutritional supplements to be tested using strict Food and Drug Administration guidelines to determine its safety and effectiveness. Georgetown doctors found that 31 percent of the patients who took ENADA felt significant relief from their symptoms of fatigue.

"According to a recent, nationwide Gallop poll, seventy-five percent of Americans state that fatigue is their number one health complaint. We are demonstrating through sound scientific studies, not marketing hype, that ENADA is both safe and effective in providing energy enhancement to alleviate the symptoms of CFS, a debilitating disorder which affects half a million Americans," said Matt Fitzsimmons, president, MENUCO Corporation.

ENADA is the brand name for the only available patented, stabilized, absorbable NADH (nicotinamide adenine dinucleotide plus high-energy hydrogen). For over 60 years, research scientists have known that NADH, a natural coenzyme derived from vitamin B3, plays an important role in the body's cellular energy-producing function. The substance occurs naturally in the muscle tissue of fish, poultry and cattle—key food sources in the human diet. But due to factors such as cooking and processing, humans receive very little of the NADH from these sources. And until ENADA, scientists were unable to develop a stable and useful oral form of NADH. ENADA is available at fine health food stores and pharmacies, including GNC, Vitamin World and The Vitamin Shoppe. It is manufactured and packaged by Menuco through a licensing agreement with Merck Pharmaceuticals.

FREE OFFER For a free video on the CFS/ Georgetown study or for more information, call 1-800-636-8261 or visit www.enada.com.

A NUTRITIONAL SUPPLEMENT MAY HELP MANY PEOPLE OVERCOMING CHRONIC FATIGUE.

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Newsworthy Trends – 2000 USA

THE WALL STREET JOURNAL.

VOL. CCXXXVI NO. 105 EE/CP ★★★ WEDNESDAY, NOVEMBER 29, 2000 WSJ.com

Our Tired Reporter Flight-Tests a Product To Combat Jet Lag

* * *

The Trip Is as Exasperating As Science Can Devise; An Unfun Game of Hearts

By Chris Adams
Staff Reporter of The Wall Street Journal

At about seven on a Saturday morning, I am one of 11 tired and slightly irritable travelers walking off an America West red-eye from San Diego to Baltimore. In the past six hours, we have had flight delays and been subjected to electronic mind games at 30,000 feet. Now, the one thing I want is a cup of coffee.

But caffeine isn't allowed. "I tell you, I can smell Starbucks on a person's breath from five yards away," warns a young research assistant named Robert Sitarz, who for 15 hours has watched everything we put in our mouths.

We all are groggy, and that's the way it's supposed to be. In the end we are taken by van to a researcher's office in northwest Washington, where about half of us get our first dose of a dietary supplement called NADH, the others a placebo. We don't know who is getting what. The idea is to see if NADH, which stands for nicotinamide adenine dinucleotide hydrogen, mitigates the effects of jet lag.

Guinea-Pig Roundup

If so, it would be a welcome relief to bicoastal executives—and a financial boon to Menuco Corp., in New York, which sells the nonprescription stuff under the brand name ENADAlert and sponsored the research. Studies like these allow companies to plaster the phrase "clinically proven" on their packaging. So Menuco rounded up 35 guinea pigs, subjected them to hassle-filled, cross-country flights, and tested them every few hours to see whose mental acuity breaks down the fastest—the NADH users or the sugar-pill poppers.

I am one of those guinea pigs. This (yawn) is my story:

The ordeal starts the morning of the Friday flight, when a group of 11 healthy men and women, all at least 35 years old, gather in the San Diego office of an otoneurologist named Erik Viirre.

Each of us leaves a urine sample and listens to the rules: no caffeine, no alcohol, no sunlight. Our group is the third to participate in the study, each under the watchful eye of Mr. Sitarz. (The Wall Street Journal paid my expenses, and I didn't accept the $225 participant's fee.)

Looming Mystery

The trial is overseen by researchers from the University of California, San Diego and Georgetown University School of Medicine in Washington. Only after all three groups are finished will researchers "break the code" to see which pills each subject got.

Nobody among us had heard about NADH before. And, in truth, most of the people recruited in San Diego see the experiment pretty much as a free trip to Washington.

The trip is west to east since jet lag is worse flying in that direction. We're making a stop in Phoenix to ensure that the flights are as annoying as possible. We're to arrive in Washington at daybreak Saturday—theoretically just in time to catch a cab for a meeting with East Coasters who have slept all night in their own beds. The whole experiment, says Dr. Viirre, is designed to mimic "the executive's lousy business trip."

Once equipped with laptop computers, we're promptly subjected to a battery of

Please Turn to Page A10, Column 1

Continued From Page A1

rapid-fire mind games. Accuracy and speed are paramount. Quick: Is 6 + 7 - 9 greater or less than five? How about 9 - 5 + 2?

The tests take 45 minutes and will be repeated five times over a 24-hour period. We also answer a series of questions about our moods that make us feel like characters in "Snow White and the Seven Dwarfs": Are we "happy," "grouchy," "drowsy," "gloomy," "furious?"

But the "money test," in the words of Dr. Viirre, is a simple game. Shapes flash on the computer and then fade away. Our task is to hit "enter" each time a heart pops onto the screen.

Sounds easy, but not after 10 minutes. "This test is deliberately slow and boring," he warns us. The tests measure subjects' lapses of attention, which can be caused by "microsleep," in which my mind could temporarily shut down even though I am sitting in a chair, with my eyes open. "You can imagine it'll be a lot tougher at midnight," Dr. Viirre says.

During the test, my mind doesn't switch off so far as I can tell, but it does wander. Schuyler Grant, a 44-year-old physicist from San Diego, begins counting each flashing figure, eventually reaching 250 or so.

'I think you're going to get a few more 'grouchy' remarks this time,' says fireman Tom Layman.

By 3 p.m., a few participants are yawning madly. We are hustled onto vans for a trip to the San Diego airport and the flight to Phoenix. After we arrive there, we're shuttled to a hotel for dinner and more tests.

Tiramisu Snafu

As we start eating, there is a small crisis: We have been served a dessert of tiramisu.

"Don't eat that!" Mr. Sitarz commands. Tiramisu has espresso in it.

A waiter swoops down and whisks away the desserts, offering carrot cake instead.

By 11 p.m., we're back at the airport, only to find our departure is to be 90 minutes late. Most of the group sacks out on airport chairs. Terrance Kwiatkowski, a 35-year-old head and neck surgeon, changes into workout clothes and walks briskly around the airport.

We're back on the plane, finally, at 1:30 in the morning. As other passengers try to sleep, we all fire up our laptops and perform the tests again. In the middle of it all the flight attendants offer drinks that most, but not all, of us are too busy to order. By 7 a.m., Eastern time, we are back in a shuttle van, heading to the Washington offices of Dr. Gary Kay.

As we zip down the parkway, Tom Layman, a 49-year-old fire-department battalion chief from a town just outside San Diego, turns to Mr. Sitarz: "I think you're going to get a few more 'grouchy' remarks this time," he says.

Once in the office, Dr. Kay breaks open a case of vials. We each, as instructed, let four little pills dissolve under our tongues.

Rousing Fernando

Then we wait. Then we test. Then we wait some more—and we watch. While previous groups had been offered a sedate selection of "National Geographic" videos, we are given something a little more lively: "Austin Powers: The Spy Who Shagged Me." A few of us laugh at the outrageous gags, while most just stare blankly at the screen, and at least three nod off.

"Fernando," somebody calls out to one of the participants. No response. Fernando is fast asleep, his chin resting heavily on his hand.

"Fernando, wake up." No reaction.

"Fer-naaaan-do." Still nothing.

"I have a sneaking suspicion Fernando got the placebo," offers Mr. Layman, the fire chief.

A few minutes later, Fernando's chin slips off his hand, and his head drops toward his knees.

By 2 p.m., the final test battery is complete. I am pretty sure my test-taking performance has been pretty consistent throughout the 24 hours; I guess it should have been because later, when the code is broken, I learn that I was indeed given NADH.

Science and Anecdote

So did the stuff work? Well, the company's news release, due out Friday, says the NADH group "achieved significantly better performance on tests of thinking and skilled motor activity" and showed a "trend to be less sleepy than subjects who received placebo."

But a scientist's standard for statistical "significance" is more rigorous than my subjective impression. Among the participants in my group, for example nobody felt noticeably different after taking the pills. (The researchers say that's common; the idea is to restore normal performance, not to jazz anybody up.)

As for the numbers, Drs. Kay and Viirre note, in their article on the research, there were differences in the NADH and placebo groups.

On a test of "working memory," both the groups posted 93% accuracy during the first test, in San Diego. On the morning test in Washington (taken one hour after getting the pills), the performance diverged—down to 91% for the control group, up to 95% for the NADH group. A few hours later, on the last test, the placebo group was 94% accurate, the NADH group 95%.

On the "money test"—the flashing hearts—the morning test showed no differences (members of the placebo group each averaged 1.6 errors, the NADH takers 1.7, out of 45 possible "targets.") The afternoon test showed the placebo group making 2.3 errors, on average, while the NADH group made 1.1.

An "error of omission" can be important. Says Dr. Viirre: "It reminds me of the air-traffic controller who says, 'Gee boss, I got the last 100 planes in, but I just missed that one.' "

As for the "trend to be less sleepy," it wasn't strong enough to be statistically significant. Nor was the mood test, which showed almost no difference between the placebo and NADH groups.

Even so, the results were good enough for Menuco, which says it had about $20 million in retail sales of NADH, its only product, last year. The words "clinically proven relief for jet lag" have already crept into its pitch.

Prof. **Birkmayer**
Health Products

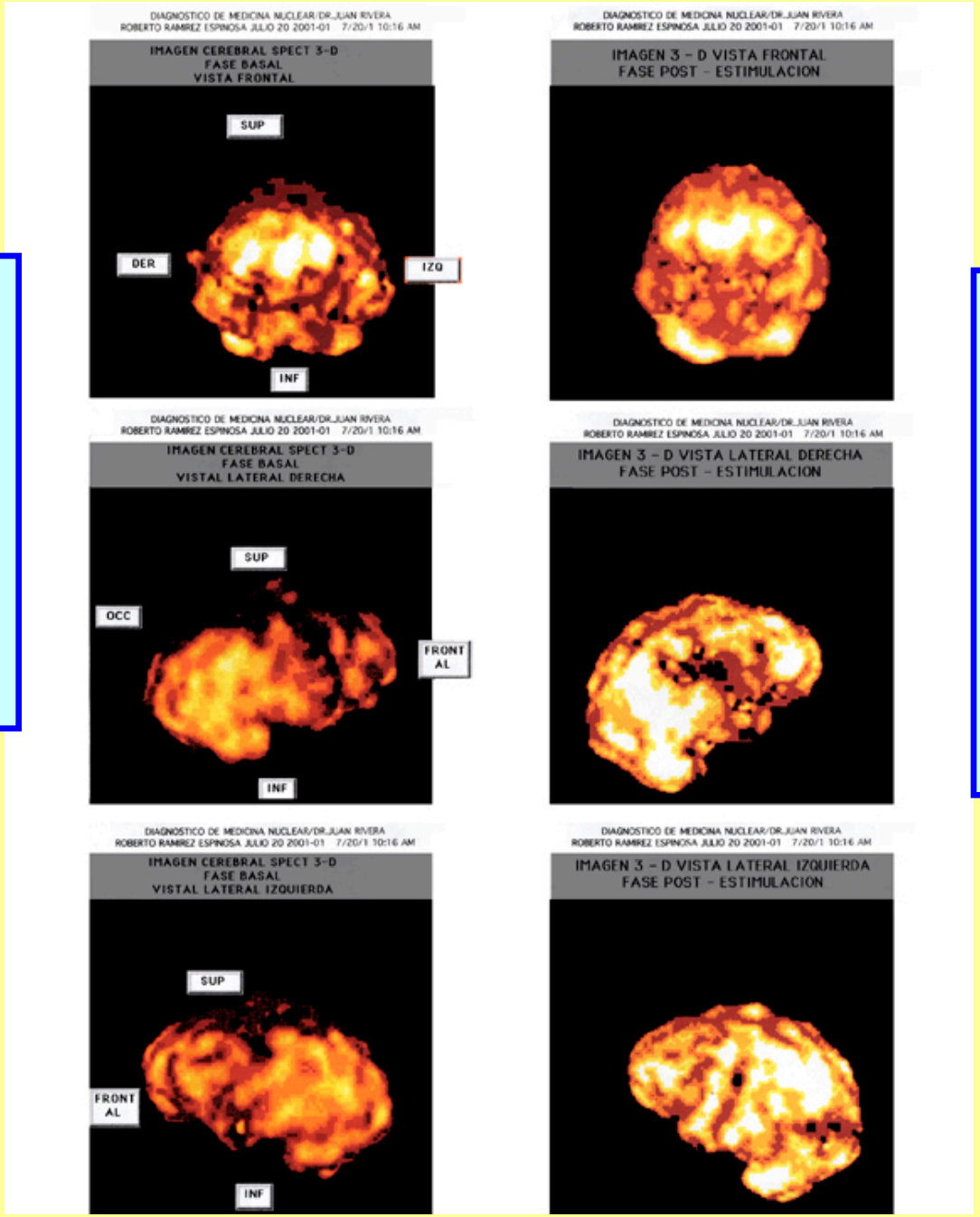
Attention Deficit Hyperactivity Disorder (ADHD)

Single Positron Emission
Computer Tomography
(SPECT – Scans)
before and 2 weeks after

ENADA® (quick acting NADH)

SPECT Scan of a 22 year old student with ADHD **before** **ENADA**

A reduced oxygen metabolism can be seen



SPECT Scan of a 22 year old student with ADHD
2 weeks after **ENADA:**

The oxygen metabolism became normal

The 2 most frequently asked questions about ENADA®

- (1) How safe is ENADA ?
- (2)Are there any side effects?

How safe is

E N A D A®

Documents submitted to the FDA

The maximum tolerated dosage of **N A D H** is **500 mg** / kg bodyweight

In other words, a person with 70 kg bodyweight can tolerate 35000 mg NADH or 7000 tablets ENADA 5mg

ENADA - NADH is one of the safest food supplement

- Long-term (6 month) safety tests in rats showed 15 mg per day per kg bodyweight is tolerated with no side effects
- 15 mg per kg corresponds to 1050 mg / day for a 70 kg subject.
- 1050 mg correspond to 105 tablets of ENADA (10 mg NADH)

No side effects have been observed

- In 6 GCP and FDA approved double blind, placebo controlled studies
- in open label studies with more than 1000 patients
- More than 500,000 consumers taking ENADA regularly since more than 5 years have not reported any side effects

Does ENADA interfere with other drugs ?

Many subjects of the studies were taking antihypertensive antidepressive and/or antihistaminic drug

No interference or side effects were observed

Suggested daily dosages for

E N A D A®

Suggested daily dosage for **ENADA**

- For more energy: 1 –2 tablets **ENADA 5mg**
- For chronic fatigue: 2 – 4 tablets **ENADA**
- **5mg**
- After sleep depriviation: 1 – 2 tablets **ENADA 10mg (= quick acting ENADA)**

Suggested daily dosage for **ENADA**

- After travelling or Jet Lag: 1 – 2 tablets
  10mg Performance (= quick acting ENADA)

- For athletic performance: 2 – 4 tablets
  20mg Mojo (=quick acting ENADA)

Experience of

ENADA®

Consumers

Consumer Responses

selected from over 900 unsolicited letters

- „Grateful and amazed with energy and stamina ENADA gives me“
- „Great, Great, Great“
- „Stunning improvement in mental&physical energy and endurance“
- „Extraordinary, fantastic“
- „Feel stronger and more sexually able“

Consumer Responses

selected from over 900 unsolicited letters

- „As a nutrional consultant I have tried every product the industry has to offer, nothing remotely compares to the dynamic power of ENADA. WOW! Thank you.“
- „Great stuff !!“
- Mental alertness much improved. Energy vastly improved after 1 month“

DR.ATKINS in his book "VITA-NUTRIENT SOLUTION"

- Page 269:
- "In this book I have not been making product recommendations by brand name, but as this writing I have found only one effective form of NADH ,

  the NADH made with
  Dr. Birkmayer's process

Earl Mindell in his "SUPPLEMENT BIBLE"

- page 110:
- **POSSIBLE BENEFITS**:
- Protects against brain aging.
- Relieves symptoms of Alzheimer's and Parkinson's disease
- Enhances ability to work out
- May increase memory and ability to concentrate

Insist on Solid Scientific Evidence of the Efficacy of Nutritional Supplements...

Before You Buy Them

More information on

ENADA® NADH

http://www.enadh.com/

http://www.enadastudies.com/