

FUNCTIONAL FOOD

**BIOBRAN**

RICE BRAN

ARABINOXYLAN COMPOUND

**GUIDE**

***Containing rice bran Arabinoxylan compound as its main component, “BioBran” is a processed food developed to provide biophylactic functions.***

Daiwa Pharmaceutical Co., Ltd. has developed foods with biophylactic functions. We have endeavored to produce food that has high activity, stability and a pleasant taste, by using hemicellulose, a type of rice bran fiber. Collaborative research with Prof. Mamdooh H. Ghoneum, Ph. D. at UCLA/Drew University in the USA has led to the development of new technologies and revolutionary new products.

# ***What is BioBran?***

## **1. Developmental Background and Function of BioBran**

### **(1) Changes in Evaluation of Food Value**

Recent studies involving food and nutritional chemistry assess the value of various foods by functional criteria - that is, by the role they serve within various physiological cycles, a trend that has gradually clarified the influence of food on health. While foodstuffs providing nutrition and attractive taste have traditionally been regarded as healthy, recent research has made it clear that food also provides other significant functions to support good health.

### **(2) Increase in Diseases of the Modern Era**

In the modern era, advanced food processing techniques have increased our consumption of refined foods such as refined rice and refined flour. Processed for improved flavor, these refined dietary staples have also been associated with increasing rates of diseases such as hyperlipidemia, diabetes, colon cancer, and ischemic heart disease, all of which now pose significant health threats.

### **(3) Discovery and Research concerning the Role of Dietary Fiber**

Although modern food refining techniques often remove fiber and other largely indigestible components, which are commonly held to impair taste, recent studies have shown that intake of fiber is closely linked to good health, albeit through actions that are quite different from those of essential nutrients. Instead, fiber maintains homeostasis and plays a therapeutic role.

After a thorough analysis of dietary fiber, we have successfully developed the Processed Vegetable Polysaccharide called "BioBran." This product is composed mainly of water-soluble dietary fiber (rice bran Arabinoxylan derivative) obtained from raw materials that form an integral part of the daily diet in Japan.

## **2. BioBran - a derivative processed dietary fiber**

BioBran is manufactured using the water-soluble dietary fiber (hemicellulose B), which constitutes about 5% of rice bran, as its main source. Rice bran hemicellulose B contains as principal ingredient Arabinoxylan, comprised of xylose and arabinose as its constitutive sugars, and has the features that its structure is included in a dietary fiber and it has a comparatively low molecular weight. Although action as an immunostimulator due to these properties was anticipated, an immunostimulating activity of the unaltered material was not demonstrable experimentally. However, the derivative which possesses immunoregulatory properties was successfully developed by partially digesting the carbohydrate of shiitake mushroom mycelia. This is a rice bran Arabinoxylan derivative. Thus, BioBran which comprises a rice bran Arabinoxylan derivative as its main ingredient, is the original food material developed through the technology of Daiwa Pharmaceutical Co., Ltd. and for which immunoregulatory function, superoxide scavenging activity, blood sugar level regulatory action, etc. have been demonstrated in many tests, unlike the natural Arabinoxylan contained in rice bran or other plants (corn, wheat, bamboo grass, etc) and the Arabinoxylan content material separated from them.

Rice bran



Hot water extract

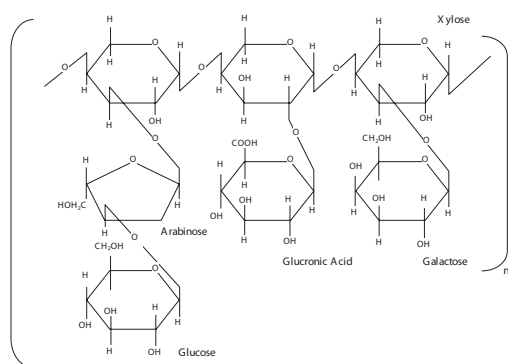
Daiwa fermentation tanks



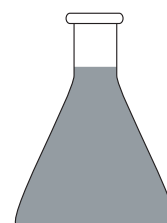
Elimination of Mycelium

Arabinoxylan, the main component  
of water-soluble dietary fiber

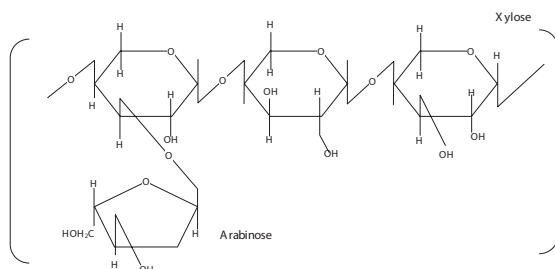
Carbohydrase Complex



Structure



## Biological modification

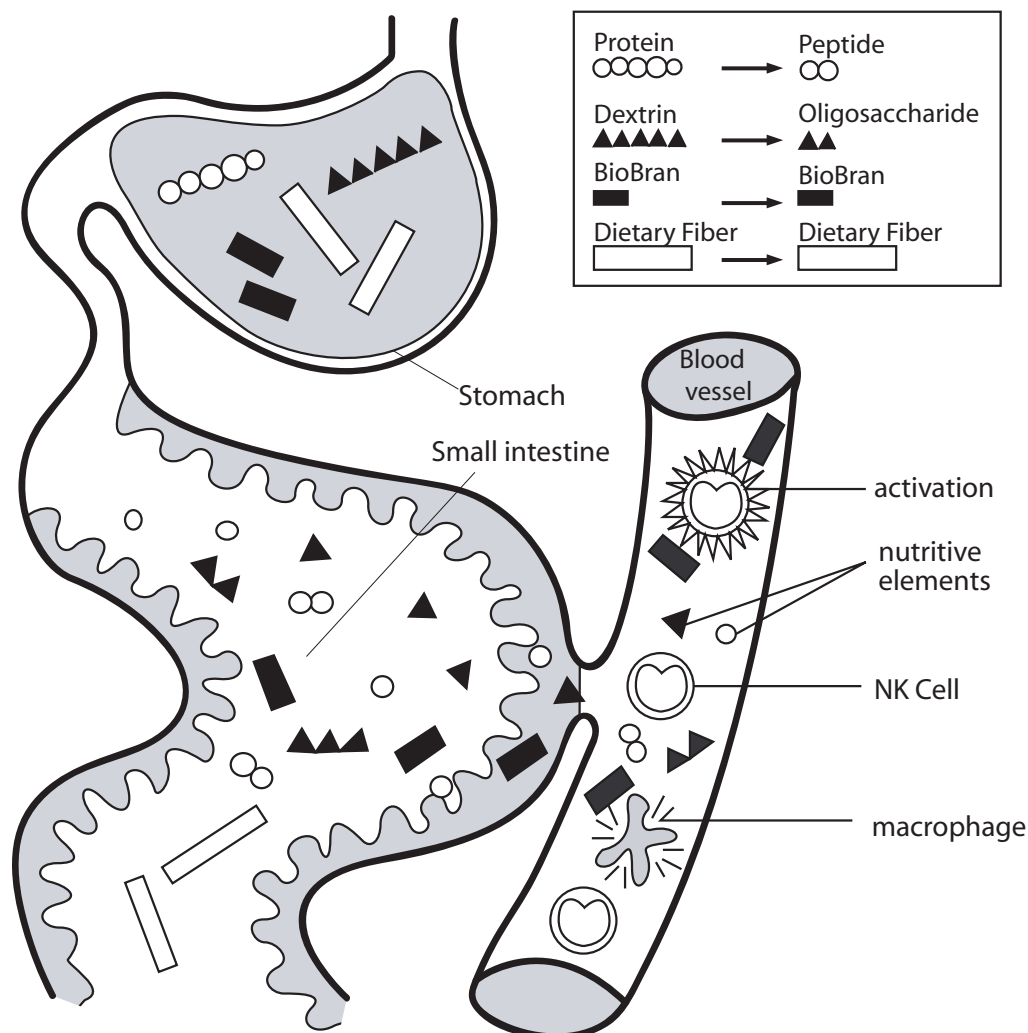


Structure

BioBran (Rice Bran Arabinoxylan Complex)

### 3. Digestion, Absorption, and Function of Dietary Fiber

BioBran partially enters the blood undigested. Proteins are digested in the stomach and in the duodenum, to be converted into peptides and amino acids, which are then absorbed in the small intestine, entering the blood to become nutritional elements. Dextrin is also digested into oligosaccharides and dextrose (glucose) and absorbed in the small intestine. BioBran is absorbed in the small intestine in undigested form and enters the blood to stimulate NK cells and macrophages. Passing through the large intestine, dietary fiber in contrast is excreted without being digested or absorbed.



## 4. Characteristics of BioBran

### (1) Characteristics

- \* BioBran has rice bran Arabinoxylan complex as its main component
- \* Light-brown powder
- \* Distinct flavor
- \* Easy to dissolve in water
- \* High and stable Immunomodulatory function

### (2) Doses

- \* Standard adult dosage: 300mg/day  
Recommended dosage of 1~3g/day for positive health maintenance

### (3) Safety

|                          |                 |
|--------------------------|-----------------|
| Mutagenicity (Ames test) | Negative        |
| Acute toxicity           | LD50 > 36g / kg |

### (4) Efficacy studies

UCLA / DREW University (USA), Cambridge University (England), McMaster University (Canada), Groningen University (Netherlands), Kobe Women's College, Nihon University, Jichi Medical School, Nagoya University, Kyoto University, Toyama Medical and Pharmaceutical University, Kawasaki Medical University, Tokyo Medical and Dental University, Chiba University, Kyushu University, etc.

## 5. BioBran Specifications

### (1) Product name

Rice Bran Arabinoxylan Compound

### (2) Source

This product is composed of dietary fiber obtained from rice bran hemicellulose B by a hot water extraction method, enzymatically broken down by the carbohydrase complex from shiitake mushrooms.

| Content Specification |         |
|-----------------------|---------|
| Carbohydrate          | 65%~80% |
| Protein               | 8%~15%  |

### (3) Characteristics

|            |                                                          |
|------------|----------------------------------------------------------|
| Color      | Light brown                                              |
| Form       | Powder                                                   |
| Scent      | Distinctive scent                                        |
| Taste      | Faint sweet taste and faint acidity.                     |
| Solubility | Water soluble<br>Over 95% soluble in water at 60°C       |
| Stability  | Stable to processing in high temperature, Hygroscopicity |

### (4) Experimental methods of confirmation

#### (a) Carbohydrate

Carbohydrate (%) = 100 - (Moisture + Protein + Lipid + Ash)

#### (b) Protein

Lowry method

#### (c) Ethanol precipitation

Precipitation of a 2% solution of the product with a fourfold dilution of absolute ethanol results in a light-brown precipitate.

(d) Wavelength of maximum absorbance

Maximum absorbance occurs at approximately 260nm and 974nm,  
as determined by spectrophotometer wavelength scanning.

(5) Moisture ..... 8% maximum

(6) Crude Ash ..... 5%~10%

(7) Arsenic (as  $\text{As}_2\text{O}_3$ ) ..... 5 ppm maximum

(8) Heavy Metals (as Pb) ..... 20 ppm maximum

(9) Aerobic plate count .....  $3 \times 10^3$  /g maximum

(10) Coliform bacteria ..... negative

(11) Mutagenicity ..... negative

(12) Acute toxicity .....  $\text{LD}_{50} > 36\text{g /kg rat}$

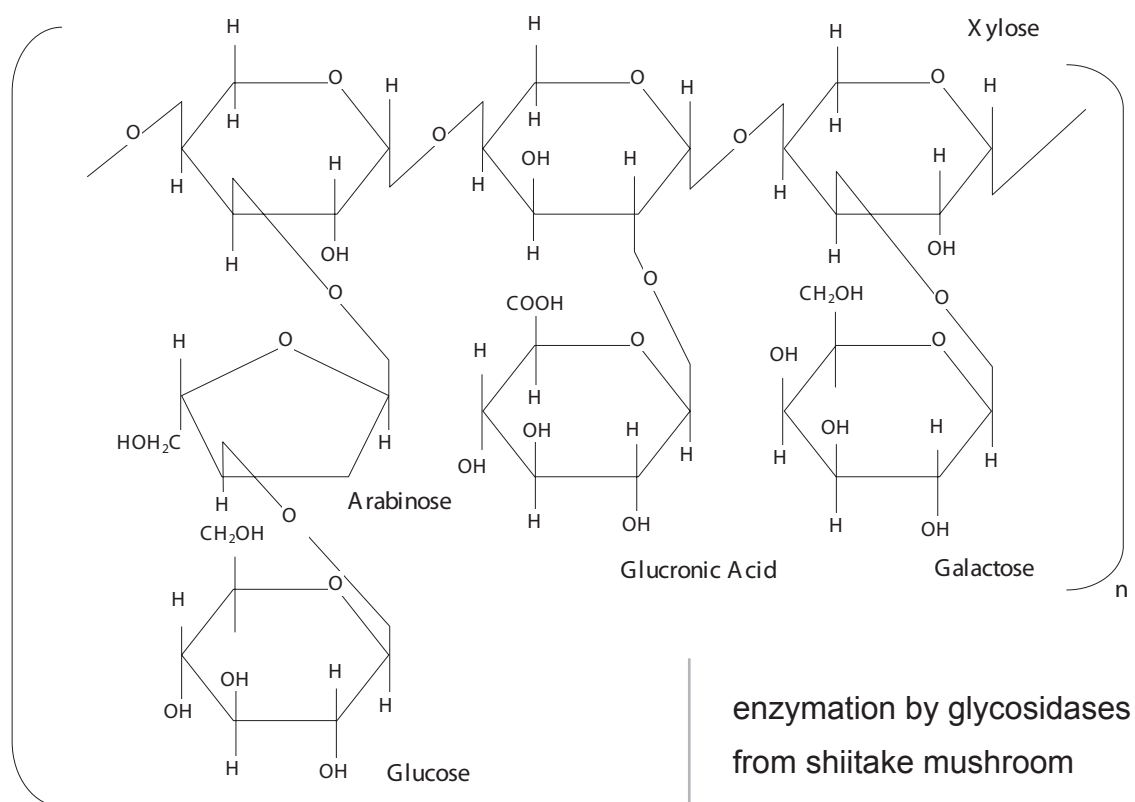
(13) Physiological activity

This product primarily influences biophylaxis systems, chiefly involving NK cells.

## 6. Effective Components of BioBran

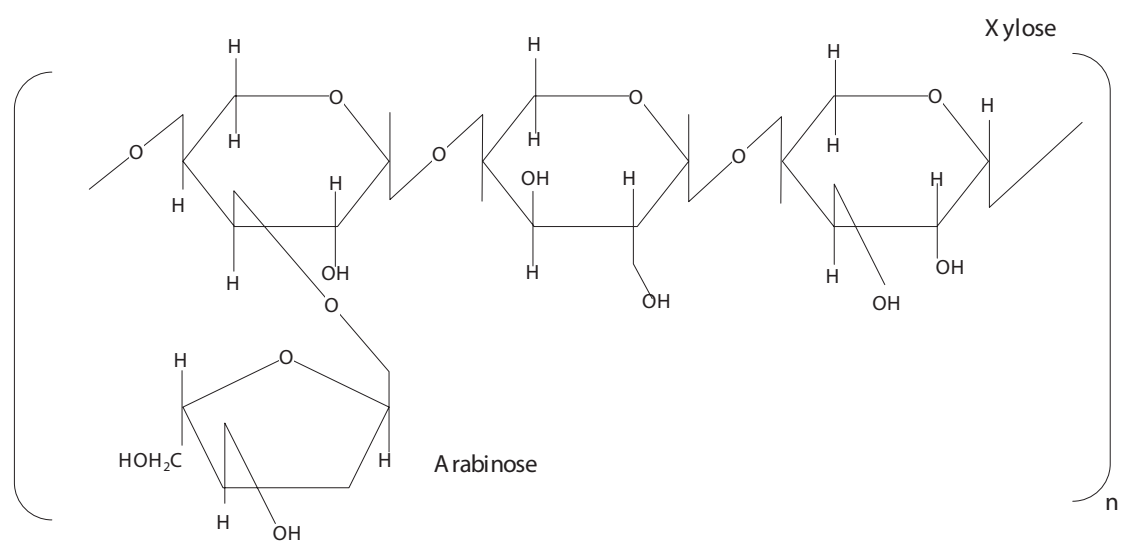
Structural Formula of Rice Bran Arabinoxylan Compound

Crude Hemicellulose model in extract of rice bran



enzymation by glycosidases  
from shiitake mushroom

Arabinoxylan Model in BioBran



## **7. The Immunopotential of BioBran (MGN-3)**

BioBran has the effect of enhancing the activities of natural immune cells such as NK cells. Enhanced NK cell activity, which is particularly important in ameliorating the effects of aging, stress and environmental pollutants, results in immunopotential. The following literature citations describe work on the relationship between dosage and period of administration on the activation of NK cells, a study of the activation of NK cells in patients with different types of cancers, and a result of research on the activation of lymphocytes including T cells and B cells.

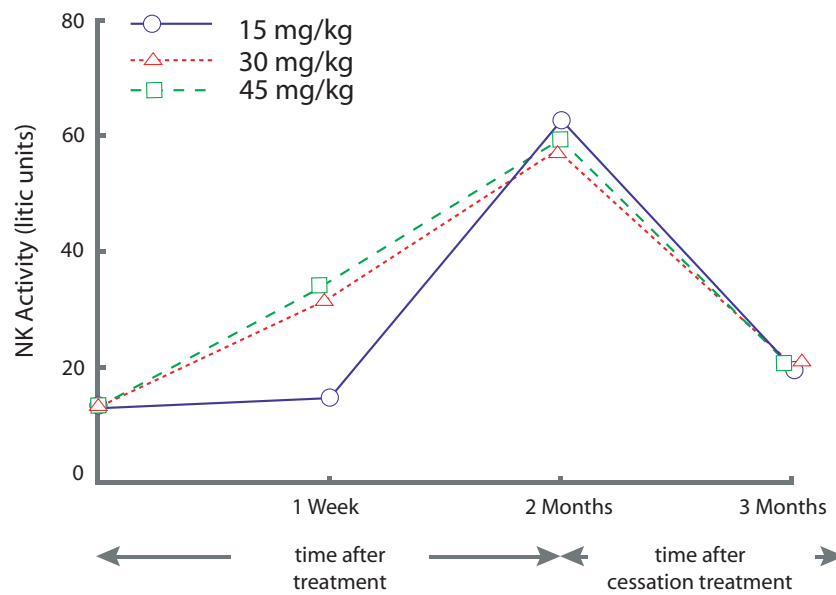
### ***Methods***

Subjects were divided into three groups of eight individuals each, who received orally administered MGN-3 over a period of two months. Groups 1, 2 and 3 received MGN-3 in doses of 15 mg/kg/day, 30 mg/kg/day, and 45 mg/kg/day, respectively. The study results were analyzed statistically.

### ***Results***

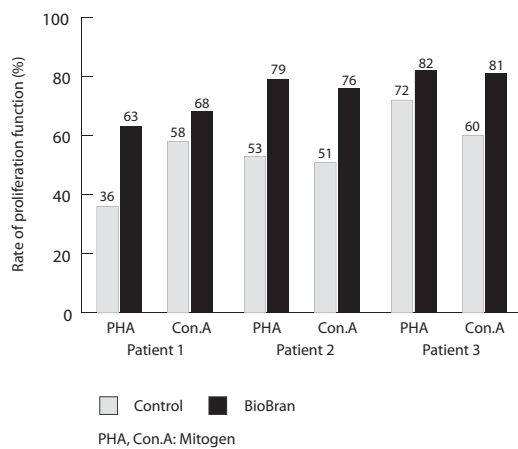
MGN-3 at a dose of 15 mg/kg/day produced no changes after one week, compared to baseline values. However, a two-fold increase in NK cytotoxicity was detected after one month of treatment. Increased dosage to 30 mg/kg/day resulted in significant enhancement of NK activity (310% over baseline), which was detected as early as one week. Peak responses were observed at the end of the treatment period (two months), when NK activity had increased fivefold. Increasing dosage to 45 mg/kg/day demonstrated similar positive trends in NK activity, but the values were higher than those for dosage of 30 mg/kg/day. Discontinuation of treatment resulted in declining NK activity, with NK activity returning to baseline levels within one month.

(Ghoneum M., Drew University. "Enhancement of human natural killer cell activity by modified Arabinoxylan from rice bran (MGN-3)", INT. IMMUNOTHERAPY XIV (2) 89-99,1998)

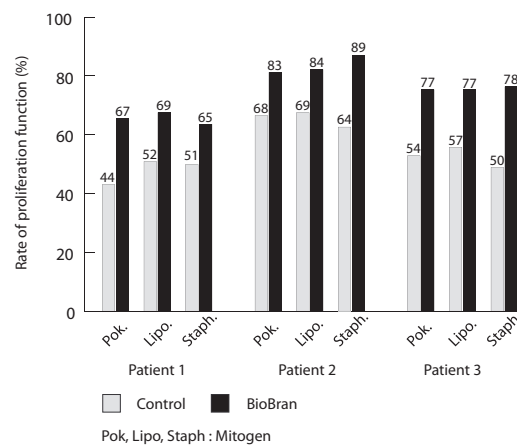


By comparing the proliferative activity of T and B lymphocytes in three individuals before and after BioBran medication, the proliferation of both T cells and B cells was found to be increased in all three after BioBran administration.  
 [Mamdooh Ghoneum, Ph. D. and Editorial supervised by Ryoichi Obitsu, Ph. D.  
 “Koganryoku (in Japanese)”, Shufunotomo Co., Ltd.]

Effect of BioBran on T cell proliferation in vivo

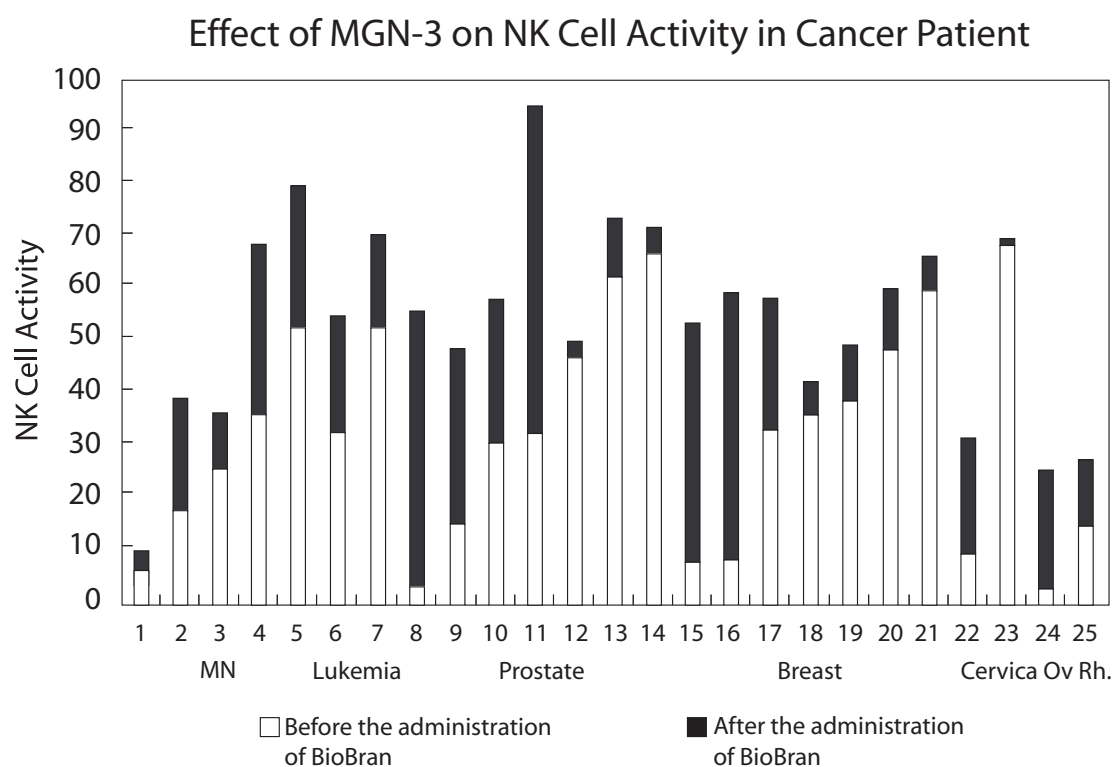


Effect of BioBran on B cell proliferation in vivo



The immunomodulatory action of BioBran was examined in 25 cancer patients with different types of advanced malignancies undergoing treatment with conventional therapy. As a result of comparing their NK cell activity before and after the 6-month administration of BioBran, all participants experienced a boost in NK cell activity after the administration.

(M. Ghoneum, "NK immunomodulatory function in 27 cancer patients by MGN-3, a modified arabinoxylane from rice bran", 87th Annual Meeting of the American Association for Cancer Research, Washington D.C., April 20-24, 1996)



## ACADEMIC RESEARCH

- 1992 Apr. Development of a physiologically active substance started using basidiomycete.
- 1995 Mar. Establishment of the extraction technology of a new physiologically active substance "MGN-3" in rice bran.  
The start of basic tests on MGN-3
- Nov. "Immunomodulatory and Anti-Cancer Properties of MGN-3, a modified xylose from rice bran, in 5 Patients with Breast Cancer"  
An AACR Special Conference in Baltimore.  
M. Ghoneum, UCLA/Drew University.
- 1996 Apr. "NK immunomodulatory function in 27 cancer patients by MGN-3, a modified arabinoxylan from rice bran"  
87th Annual Meeting of the American Association for Cancer Research (AACR). Washington DC. M. Ghoneum, N. Galal
- Jun. "Effect of human Natural Killer Cell activity and Interferon- $\gamma$  synthesis in vitro"  
ASBMB/ASIP/AAI JOINT MEETING in New Orleans.  
M. Ghoneum, UCLA/Drew University
- Jul. "Anti HIV activity by MGN-3 in vitro"  
11th International AIDS Conference in Vancouver.  
M. Ghoneum, UCLA/Drew University
- 1997 Sep. "The Effect of MGN-3, an Arabinoxylan Compound, on Serum Lipids in Streptozotocin Induced Diabetic Rats."  
38th American Meeting of Nutrition Annual Meeting, New York, USA  
Ohara I., Tabuchi R., Maeda H., Faculty of Home Economics, Kobe Women's University, Kobe, JAPAN and Daiwa Pharmaceutical Co.,

Ltd., Tokyo, JAPAN

- 1998 Jun. "MGN-3 Immunotherapy for the Treatment of Cancer"  
The First international Symposium on Disease Prevention by IP6 &  
Other Rice Components, Kyoto, JAPAN.  
Ghoneum M., Maeda H., Department of Otolaryngology, Drew  
University of Medicine and Science, LA, USA, and Daiwa  
Pharmaceutical Co., Ltd., Tokyo, JAPAN
- Aug. "Human NK Activity and Synergism of a low dose of IL2 $\alpha$  and a  
Modified Rice Bran Arabinoxylan on a Generation of TNF $\alpha$ "  
Conference of Anti-Aging Mechanism.  
Ghoneum M., Gewet A., NJ. USA
- Sep. "NK cell activity by MGN-3"  
26th Academy of Alternative Medicine of Cancer in LA  
Ghoneum M., UCLA/Drew University, USA
- Oct. "Immunopotential by utilization of MGN-3 tissue"  
Congress on Anti-Aging Medicine in Nevada  
Ghoneum M., UCLA/Drew University, USA
- Nov. "NK Immunorestitution of Cancer Patients by MGN-3, a Modified  
Arabinoxylan Rice Bran (Study of 32 patients up to 4 years)"  
6th International Congress on Anti-Aging & Bio-Medical  
Technologies.  
Ghoneum M., UCLA/Drew University
- Dec. "Evaluation of Processed Vegetable Polysaccharide Food, Bio Bran  
on Superoxide Scavenging Activity"  
3rd JsoFF Conference  
Tazawa K., Toyama Medical and Pharmaceutical University, Maeda  
H., Daiwa Pharmaceutical Co., Ltd.

- 1999 Jul. "A case study of supplementary application of rice bran  
Arabinoxylan (MGN-3) to bone metastasis from lung cancer"  
2nd Conference of Japanese Association for Alternative,  
Complementary and Traditional Medicine (JACT), Tokyo, JAPAN  
Sobajima T., Hoshigaoka Welfare Annuity Hospital, Maeda H.,  
Daiwa Pharmaceutical Co., Ltd., Tokyo
- Jul. "Evaluation of MGN-3 (Bio Bran) on Superoxide Scavenging  
Activity"  
6th Japanese Conference on Cancer Prevention, Tokyo Japan  
Tazawa K., Namikawa H., Oida S., Ito K., Yatsuzuka M., Koike J.,  
Maeda H.<sup>\*</sup>, Toyama Medical University, Daiwa Pharmaceutical Co.,  
Ltd.<sup>\*</sup>
- Dec. "Evaluation of MGN-3 (Bio Bran) with activation function of NK cell  
activity on Superoxide Scavenging Activity"  
12th Japanese Conference on Bio Therapy, Yokohama, Japan  
Tazawa K., Namikawa H., Oida S., Ito K., Yatsuzuka M., Koike  
J., Masada M.<sup>\*</sup>, Maeda H.<sup>\*\*</sup>, Toyama Medical University, Chiba  
University<sup>\*</sup>, Daiwa Pharmaceutical Co., Ltd.<sup>\*\*</sup>
- Dec. "Application of Modified Rice Bran Dietary Fiber to Diabetes and  
Taste Preference in Streptozotocin-Included Diabetic Rats"  
2nd International Conference on Food Factors, Kyoto, Japan  
Ohara I., Onai K., Maeda H.<sup>\*</sup>, Laboratory of Nutrition, Faculty of  
Home Economics, Kobe Women's University, Daiwa Pharmaceutical  
Co., Ltd.<sup>\*</sup>
- Dec. "Immunostimulation and Cancer Prevention"  
7th International Congress on Anti-Aging & Biomedical  
Technologies, Las Vegas, USA, Ghoneum M. Ph. D., Drew  
University
- 2000 Jan. "Physiological Activator, Oryza Sativa L. Arabinoxylan Derivate

(MGN-3)”

6th Conference of Japan Mibyou System Association, Hiroshima,  
Japan,

Maeda H., Daiwa Pharmaceutical Co., Ltd.

Jun. “The Effect of MGN-3 on Cisplatin and Adriamycin Induced Toxicity  
in the Rat”

American Society for Pharmacology and Experimental

Therapeutics, Boston, USA, Jacoby H., Wnorowski G., Sakata K.\*,  
and H. Maeda\*\*, Product Safety Lab.

Creative Strategy\*, Daiwa pharmaceutical Co., Ltd.\*\*

Oct. “Inhibitory effects of MGN-3 (modified Arabinoxylan from rice bran)  
on free radical”

The 59th Annual Meeting of the Japanese Cancer Association,

Yokohama, Japan, Saito T., Ohkami H., Tsukada K., Tazawa K.,

Namikawa H., Oida S., Koike J., Yatsuzuka M., Masada M.\*, and

H. Maeda\*\*, Toyama Medical University, Chiba University\*, Daiwa  
Pharmaceutical Co., Ltd.\*\*

Nov. “Evaluation of Immune (Arabinoxylan) therapy seen from NK cell  
activity and the CD4/CD8 ratio on cancer patients”

The 3<sup>rd</sup> Annual Meeting of the Japanese Society for Complementary  
& Alternative Medicine & Treatment, Tokyo, Japan

2001 Jan. “Application to the alternative medicine of a new physiological active  
substance “Arabinoxylan derivative” (MGN-3, Bio Bran)”

7<sup>th</sup> Conference of Japan Mibyou System Association, Nagoya,  
Japan

Maeda H., Daiwa Pharmaceutical Co., Ltd.

Jul. “Inhibitory effect of MGN-3 on the progress of atopic dermatitis in  
NC mice”

11<sup>th</sup> International Congress of Immunology, Stockholm, Sweden

Nonoyama S., Lin L., Tokyo Medical and Dental University

2002 Mar. "Study on the growth inhibiting component of cancerous cells in culture cell lines derived from modified rice-bran arabinoxylan"  
46<sup>th</sup> Japan Society for Bioscience, Biotechnology, and Agrochemistry, Sendai, Japan  
Miyazaki F., Hashizume T.\*, Kodama H.\*\* , Maeda H.\*\*\* and M. Masada\*\*, Technology Department, Kazami Co., Ltd.\* , Department of Bioresources Chemistry, Faculty of Horticulture, Chiba University\*\*, Daiwa Pharmaceutical Co., Ltd.\*\*\*

Mar. "The effect of modified rice-bran arabinoxylan on NK activity of human peripheral blood lymphocytes"  
46<sup>th</sup> Japan Society for Bioscience, Biotechnology, and Agrochemistry, Sendai, Japan  
Shimomura C., Ueda Y.\* , Kodama H.\* , Maeda H.\*\* and M. Masada\*, Department of Bioresources Chemistry, Faculty of Horticulture, Chiba University\*, Daiwa Pharmaceutical Co., Ltd.\*\*

2002 Oct. "Normalization of the Lymphocyte System in Peripheric Blood Reaction by Arabinoxylan from Rice Bran (MGN-3)"  
43<sup>rd</sup> Annual Meeting, American College of Nutrition, San Antonio, Texas, Ueda Y.\* , Masada M. \* and H. Maeda\*\*, Department of Bioresources Chemistry, Faculty of Horticulture, Chiba University\*, Daiwa Pharmaceutical Co., Ltd.\*\*

Oct. "MGN-3 potentiates death receptor-induced apoptosis in cancer cells"  
93<sup>rd</sup> Annual Meeting 2003 of American Association for Cancer Research, Boston, USA  
Ghoneum M. and S. Gollapudi, Drew University of Medicine and Science, Los Angeles, CA, UC Irvine, Division of Basic and Clinical Immunology, Irvine, CA

- Nov. "Effect of Enzyme-processed Rice Bran Hemicellulose (MGN-3) on Experimental Liver Dysfunction in Rats"  
7<sup>th</sup> Conference of Japanese Association for Dietary Fiber Research,  
Tokyo, Japan  
Yamada T.\*, Daizou A.\*, Poindoglun K.\*, Egashira K.\*\*, Maeda H.\*\*\* and H. Sanada\*\*, Graduate School of Science and Technology, Chiba University\*, Department of Bioresources Chemistry, Chiba University\*\*, Daiwa Pharmaceutical Co., Ltd.\*\*\*
- Nov. "Significance of asthmatic mouse model exposed to antigen (Toluene Diisocyanate) for a prolonged period"  
52<sup>nd</sup> Conference of Japanese Society of Allergology, Yokohama, Japan  
Kanbayashi H. and Y. Endo, Department of Pathological Molecular Medicine, McMaster University
- Nov. "Evaluation of the effects of asthma prevention and symptom reduction by enzymatically modified rice-bran foods in asthmatic model mice"  
52<sup>nd</sup> Conference of Japanese Society of Allergology, Yokohama, Japan  
Kanbayashi H. and Y. Endo, Department of Pathological Molecular Medicine, McMaster University
- 2003 Sep. "Effect of BIOBRAN proved by Scientific Studies"  
Japanese Academy for Clinical Complementary & Alternative Medicine, Maeda H., Daiwa Pharmaceutical Co., Ltd.
- Oct. "Immunoactivation therapy for various progressive cancers using rice bran arabinoxylan derivative (Bio Bran)"  
The Japanese Society for Complementary and Alternative Medicine,  
Tsunekawa H. and H. Maeda

Dec. "The orally administration of the Hydrolysis Rice Bran prevents a common cold syndrome for elderly people based on immunomodulatory function"  
Medical and Pharmaceutical Society for WAKAN-YAKU  
Maeda H., Omura K. and X. Zhu, Daiwa Pharmaceutical Co., Ltd.

Dec. "The effect in the physiological function of a Modified Arabinoxylan Rice Bran", Japan Society for Biological Therapy  
Masada M., Maeda H. and K. Tazawa, Chiba University, Daiwa Pharmaceutical Co., Ltd, Toyama Medical University

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The Abstract of Bio Bran Workshop in Berlin, 2002
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Glucose Tolerance in NIDDM Adult Rats Given Streptozotocin as  
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NIDDM Adult Rats Given Streptozotocin as Neonates." *Aichi  
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Serum Lipids and Taste Preference in Streptozotocin-Induced  
Diabetic Rats.", *Nutrition Research*, Vol.20, No.1, pp. 59-68.
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"The Orally Administration of the Hydrolysis Rice Bran Prevents  
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The Abstract of Bio Bran Workshop in Berlin, 2002
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Tokyo, Japan.



**DHD(*Europe*)Ltd.**

Arabinoxylan Compound from Rice Bran is produced by Daiwa Pharmaceutical Co. Ltd, Japan  
BioBran is imported and distributed by DHD(*Europe*)Ltd., Cambridge, UK

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