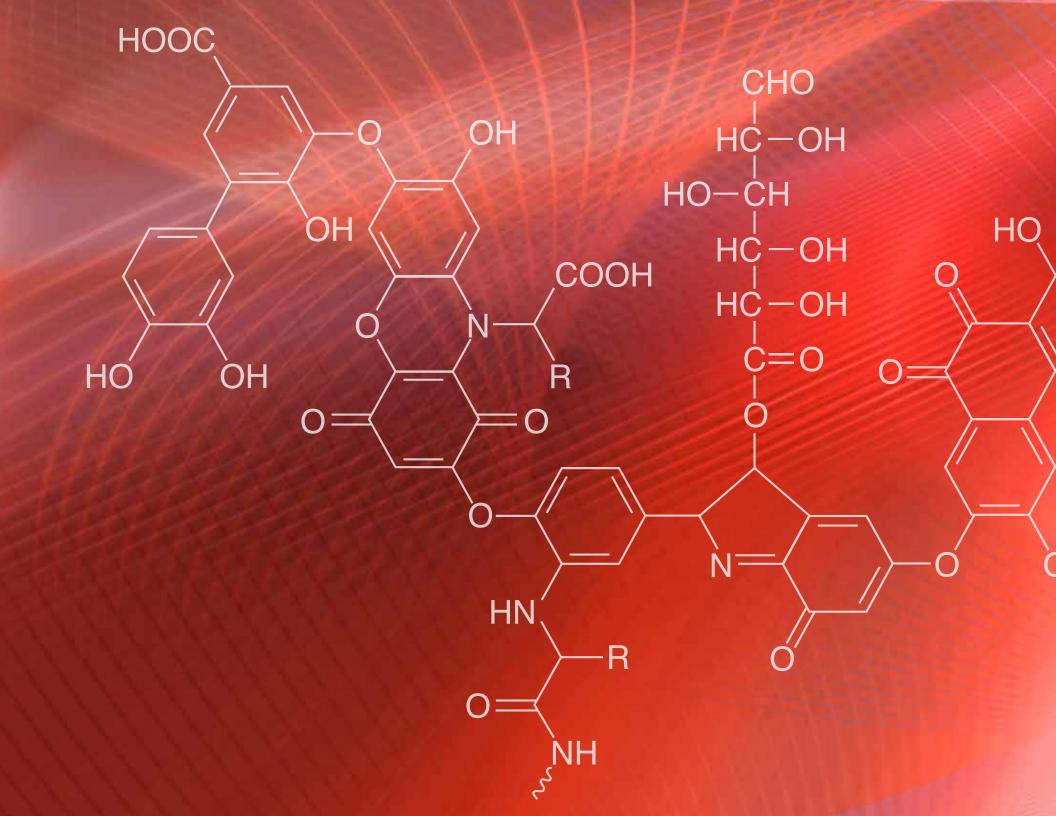


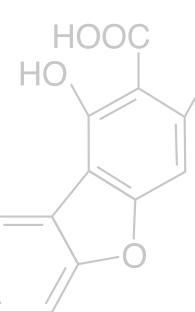
# HUMIC HEALTH RESEARCH MILESTONES

From Mother Earth.

All Natural.

Perfect.





### COOH

**Humic** substances are ubiquitous materials that arise from natural processes, such as prolonged biochemical degradation of plant residues. Humic acid and humates (the salt-form) occur in soils, sediments, coal, and water. Approximately 40-60% of dissolved organic carbon (DOC) in freshwaters and 60-70% of total soil carbon are comprised of humic materials, representing the largest reservoir of carbon in the biosphere.

The first "western" scientific study of humic acid was reported in 1786 by F. K. Achard (Crell's Chem. Anal. 1786, 11, 391-403). However, clays, soils, and other earths (such as "shilajit") have been in pharmacological use in "eastern" medicinal practice for far longer (R. Root-Bernstein and M. Root-Bernstein, Honey, Mud, Maggots, and Other Medical Marvels; Boston: Mariner Press, 1998; Ch. 5).

Modern research has shown that humic acid contains a wide range of essential minerals and other vital nutrients necessary for human health. It is also highly effective in supporting a healthy immune system, especially during seasonal times of occasional microbial challenge.\*

\*This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

## **SAFETY**

### **JANUARY 1989 - SAFETY IN MAMMALS**

Humic acids derive from a class of natural humic substances. The chemical properties of certain defined humic acid products impel their application in diseases of the digestive system of mammals when complicated by metabolic disorders, particularly in stages of early growth. Their simple administration (via feed), exceptional safety, and the absence of side effects (e.g., allergy, resistance) — as well as no residue formation in animal-derived products-support the broad application of these substances in veterinary medicine.

M. Kuhnert, V. Fuchs, and S. Golbs. Pharmacologic and Toxicologic Properties of Humic Acids and Their Activity Profile for Veterinary Medicine. DTW Deutsch. Tierarzt. Woch. 1989, 96(1), 3-10.

### **APRIL 1993 - SYSTEMIC TOLERATION**

The systemic toxicity of the peat (humic acid) preparation TPP in rats and rabbits was assessed. Dermal irritation tests were conducted on rabbits. In acute and chronic toxicity studies TPP was well tolerated in both animal species. Laboratory findings revealed no hematologic abnormalities nor disturbances in liver or kidney functions. No local irritancy of TPP was observed. The results show that TPP humic acid may be considered as essentially nontoxic.

H. Czyzewska-Szafran, Z. Jastrzebski, et al. Systemic Toxity and Dermal Irritation of Tolpa Peat Preparation. Acta Pol. Pharm. 1993, 50(4), 373-377.

### **JUNE 1993 - IMMUNE PARAMETERS**

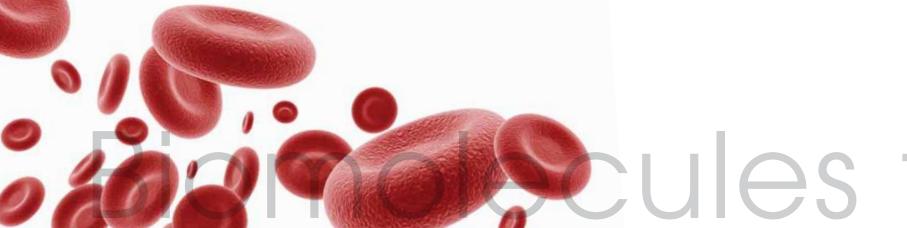
Investigations were carried out on selected immune parameters in healthy humans receiving humic acid (TPP) in doses of 50, 100, 300, and 600 mg daily for 14 days. A 50-mg dose of TPP changed neither the T-cell percent among mononuclear cells nor the composition of T-cell subsets. A dosage of 100 mg caused a significant increase in the percent of T-cells on the 14th day but did not influence their subset composition. In doses of 50 and 100 mg, a slight immunomodulatory potential was observed in healthy humans.

Z. Baj, K. Zeman, Z. Sulowska, et al. Effect of (Humic Acid) Tolpa Peat Preparation on Some Immune Parameters in Healthy Volunteers. Preliminary Data. Acta Pol. Pharm. 1993, 50(6), 481-489.

### **JANUARY 2002 - PHASE I TRIALS**

The objective of the 2-week study was to evaluate the safety and toxicity profile of humic acid at various doses in HIV-1-infected individuals. All active treatment groups gained weight compared to the placebo. None of the biochemical and hematological parameters measured differed significantly from the baseline at the end of treatment. Humic acid was therefore judged well tolerated with an excellent safety profile.

M. E. Botes, J. Dekker, and C. E. J. van Rensburg. Phase I Trials with Oral Oxihumate in HIV-Infected Patients. Drug Devel. Res. 2002, 57(1), 34-39.



### **PHARMACOLOGY**

### **JULY 2001 - MEDICAL ASPECTS**

Humic substances (HS) comprise one of the largest reservoirs of carbon in nature. This review focuses on the medical and veterinary-medical applications of humics, followed by a discussion of several aspects of environmental health.

R. Kloecking and B. Helbig. Medical Aspects and Applications of Humic Substances. Biopolymers 2001, 1, 379-392.

### **FEBRUARY 2002 - HUMIC DRUGS**

A review of medicinal drugs from humus matter (such as peat, sapropel, and mumie), including Shilagen, Abana, Cystone, Diabecon D-400, EveCare, Geriforte, Lukol, Pilex, Rumalava, Tentex forte, Nefrotec, Adrenotone, Diotone, La-Tone Gold, Andro-Surge, and Solanova Libidoplex. Therapeutic extracts of humic acids are antibacterial, antitoxic, antiradical, antiulcerogenic, antiarthritic, immunomodulatory, and antiinflammatory.

I. Schepetkin, A. Khlebnikov, and B. S. Kwon. Medical Drugs from Humus Matter. Drug Devel. Res. 2002, 57, 140-159.

#### MARCH 2003 - IMMUNOPHARMACOLOGY

(Humic acid) increased the proliferative response of phytohaemagglutinin-stimulated human lymphocytes, which response was even more striking in lymphocytes from HIV-infected patients. The response is associated with an increased production of IL-2, as well as expression of the IL-2 receptor in the setting of decreased production of IL-10.

G. K. Joone, J. Dekker, et al. Investigation of the Immunostimulatory Properties of Oxihumates. Z. Naturforsch. C: J. Biosci. 2003, 58(3/4) 263-267.

### **JANUARY 2005 - BIOMEDICINE**

Humic substances as part of humus-soil organic matter are compounds arising from the physical, chemical, and microbiological transformation (humification) of biomolecules. They are important because they constitute the most ubiquitous source of non-living organic material known in nature.

E. M. Pena-Mendez, J. Havel, and J. Patocka. Humic Substances-Compounds of Still Unknown Structure: Applications in Agriculture, Industry, Environment, and Biomedicine. J. Appl. Biomed. 2005, 3, 2-12.

### FEBRUARY 2005 - PHYSIOLOGY

Humic acids and their salts and related derivatives have an extended spectrum of physiological activities. They also exhibit various pharmacological effects. Data on the preparation of brown coal humic acids are given, and their anthelmintic activity is demonstrated in mice.

Sh. Zh. Zhorobekova, R. P. Koroleva, and N. K. Alybakova. About the Physiological Activity of Humic Acids. Izv. Nats. Akad. Nauk Kyrgyz. Resp. 2005, (2), 18-21.

### **DECEMBER 2006 - PHARMACOLOGICAL ACTIVITY**

Classification and chemical and physical properties of humic acids are described. Mucosa-regenerating, antiresorptive, adsorptive, fungicide, bactericide, virucide, antiphlogistic, and digestive effects are summarized. Toxicity and medical applications are included.

M. Kuehnert and H. Knauf. Humic Acids for Oral Application. Deutsch. Apoth. Z. 2006, 146(49), 101-104.

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## **APPLICATIONS**

### MARCH 2004 - ANTI-INFLAMMATORY

Exposure of resting and PMA-stimulated human neutrophils to potassium humate resulted in a decreased expression of CR3 by activated, but not resting cells, in a dose-related way. Humate also inhibited the adhesion of PMA-stimulated neutrophils to a baby hamster kidney cell line expressing ICAM1 (the CR3 ligand). Similar results were obtained using normal BHK cells. Because humate is well tolerated with an excellent safety profile it merits further evaluation in patients suffering from inflammatory conditions.

G. K. Joone and C. E. J. van Rensburg. An In Vitro Investigation of the Anti-Inflammatory Properties of Potassium Humate. Inflammation 2004, 28(3), 169-174.

### JANUARY 1993 - DOUBLE-BLIND STUDY

A randomised, double-blind study to assess the therapeutic efficacy of humic acid for recurrent respiratory tract infections was carried out on 39 patients aged 16-22. Five mg was administered orally for 3 weeks. During the 3-month follow-up period favourable therapeutic results were obtained in 14 of 20 treated patients and in 8 of 19 placebo patients. Therapeutic effects were observed even after the 6-month follow-up period. The phagocytic activity of granulocytes was significantly stimulated in the treated patients but not in the placebo-treated patients. The results suggest that humic acid is an effective medicament for the treatment of recurrent respiratory tract infections with undefined infectious etiology. No side effects were observed either during the treatment period or during the 6-month follow-up period.

A. Jankowski, B. Nienartowicz, et al. A Randomized, Double-Blind Study on the Efficacy of Tolpa Torf Preparation (TTP) (Humic Acid) in the Treatment of Recurrent Respiratory Tract Infections. Arch. Immunol. Therap. Exper. 1993, 41(1), 95-97.

### FEBRUARY 2002 - INFLUENZA

Two synthetic humic acids and one natural-product humic acid were found to inhibit the in vitro replication of influenza virus A/WSN/33 (H1N1) in Madin-Darby canine kidney (MDCK) cells at concentrations of no cytotoxicity. The materials inhibited virus-induced hemagglutination and low pH-induced cell-cell fusion; and also the endonuclease activity of viral RNA polymerase.

F. J. Lu, S. N. Tseng, et al. In Vitro Anti-Influenza Virus Activity of Synthetic Humate Analogues Derived from Protocatechuic Acid. Arch. Virol. 2002, 147(2), 273-284.

### 2002/2004 - AIDS IN VITRO

Oxihumate inhibited HIV-1 infection of MT-2 cells with an IC50 value of  $12.5 \,\mu g/mL$  Treatment of free and cell-attached HIV with oxihumate irreversibly reduced infectivity, while the susceptibility of target cells to the virus was not impaired by treatment prior to infection. Infectivity inhibition was due to interference with CD4 binding and the V3 loop-mediated step of virus entry. No viral resistance to oxihumate developed over a 12-week period in vitro.

C. E. J. van Rensburg, J. Dekker, et al. Investigations of the Anti-HIV Properties of Oxihumate. Chemotherapy 2002, 48(3), 138-143.

The IC50 values of a humic acid derivative against an HIV-1 T-tropic laboratory strain and an M-tropic AZT-resistant wild-type strain were 0.85 and 3.5  $\mu$ g/mL, respectively. The combination of humic acid and AZT intensified the anti-viral activity 30-100 times. The p24 HIV-1 antigen value of the first passage virus generation in the presence of 0.0025  $\mu$ g/mL of compound was identical to that of the control while the infectious activity approached zero. Successive viral generations exhibited low values of p24 HIV-1 antigen and showed undetectable infectious activity.

G. Kornilaeva, A. Becovich, et al. New Humic Acid Derivative as Potent Inhibitor of HIV-1 Replication. Med. Gen. Med. 2004, 6(3), A10360.

# Biomolecules fro

### **APRIL 2002 - HERPES**

Polymeric (humic acid) products showed anti-HSV-1 IC50 values in the range of 0.65-322  $\mu$ g/mL. Functional group analysis revealed that increasing numbers of carboxyl groups together with a high content of hydroxyl groups tended to enhance polymer antiviral activity.

R. Kloecking, B. Helbig, G. Schotz, et al. Anti-HSV-1 Activity of Synthetic Humic Acid-Like Polymers Derived from p-Diphenolic Starting Compounds. Arch. Chem. Chemother. 2002, 13(4), 241-249.

### **APRIL 2002 - TOPICAL APPLICATIONS**

The study objectives were to establish first the safety and second the therapeutic efficacy of topically applied oxifulvic acid compared to 1% hydrocortisone and placebo creams. Oxifulvic acid has previously been demonstrated to exhibit anti-inflammatory properties in vitro, and also the inhibition of elicited ear inflammation in mice at concentrations of 4.5% and 9%. In this double-blind cross-over study, 23 healthy volunteers allergic to grass or house dust mite allergen were randomized to receive either 4.5% or 9% oxifulvic acid for 2 weeks on the volare aspect of one forearm (100 mm diameter) and rechallenged 21 days later to establish sensitization. Thereafter, patients were randomized to either placebo, 1% hydrocortisone, or 4.5% or 9% oxifulvic acid creams. Topically applied oxifulvic acid had no significant effect on any safety parameters and also did not induce sensitization when applied on the skin. Oxifulvic acid inhibited the elicited inflammatory reaction in as little as 15 min; the 9% cream was significantly more effective than the 4.5% cream at 24 h. Overall efficacy was similar to that shown by hydrocortisone.

J. R. Snyman, J. Dekker, S. C. K. Malfeld, et al. Pilot Study to Evaluate the Safety and Therapeutic Efficacy of Topical Oxifulvic Acid in Atopic Volunteers. Drug Devel. Res. 2002, 13(4), 241-249.

#### **OCTOBER 2007 - RHEUMATOID CONDITIONS**

Mud, which contains organic and mineral ingredients, is a well-known treatment for several degenerative diseases. The chemical structure of mud not only contains hydrophilic organic substances, such as humic, fulvic, and ulmic acids, but also low-molecular-weight organic substances mostly comprised of fatty acids.

E. Odabasi, H. Gul, E. Macit, et al. Lipophilic Components of Different Therapeutic Mud Species. J. Altern. Complem. Med. 2007, 13(10), 1115-1118.

### **OCTOBER 2007 - TUMOR SUPPRESSION**

A humus extract exhibited an antitumor effect on L1210 tumor development in isogenic DBA/2 mice. Tumor formation was delayed and a significant smaller tumor mass resulted with humic treatment, resulting in a significant increase in the lifespan of the mice. The antitumor effect was not due to direct killing of L1210 or induction of apoptosis in tumor cells.

H. Kodama. Antitumor Effect of Humus Extract on Murine Transplantable L1210 Leukemia. J. Vet. Med. Sci. Jpn. Soc. Vet. Sci. 2007, 69(10), 1069-1071.

### **DECEMBER 2004 - OF PARTICULAR INTEREST**

The (humic acid) compositions are efficacious for the treatment or prophylaxis of infections, in particular HIV/AIDS; and for the enhancement of immunity. Special uses relate to reducing risks of mother-to-child transmission and treating HIV-positive pregnant women.

W. J. Serfontein. Nutritional Compositions and Use Thereof as Anti-HIV and Anti-AIDS Nutraceuticals and Immunostimulants. WO 2004/107,881 (December, 2004).

