Collection of Health/Medical Abstracts Sourced through PubMed

By: Michael Karr, Ph.D.

Note: Relevant passages of abstracts are bolded for quicker reading. Some abstracts have my comments after them in this font (Comic Sans MS)

1: Appl Environ Microbiol. 2008 Apr;74(7):2004-15. Epub 2008 Feb 1.

Rapid growth of planktonic Vibrio cholerae non-O1/non-O139 strains in a large alkaline lake in Austria: dependence on temperature and dissolved organic carbon quality.

Kirschner AK, **Schlesinger J**, **Farnleitner AH**, **Hornek R**, **Süss B**, **Golda B**, **Herzig A**, **Reitner B**.

Clinical Institute of Hygiene and Medical Microbiology, Water Hygiene, Medical University Vienna, Kinderspitalgasse 15, 1095 Vienna, Austria. alexander.kirschner@meduniwien.ac.at

Vibrio cholerae non-O1/non-O139 strains have caused several cases of ear, wound, and blood infections, including one lethal case of septicemia in Austria, during recent years. All of these cases had a history of local recreational activities in the large eastern Austrian lake Neusiedler See. Thus, a monitoring program was started to investigate the prevalence of V. cholerae strains in the lake over several years. Genetic analyses of isolated strains revealed the presence of a variety of pathogenic genes, but in no case did we detect the cholera toxin gene or the toxin-coregulated pilus gene, both of which are prerequisites for the pathogen to be able to cause cholera. In addition, experiments were performed to elucidate the preferred ecological niche of this pathogen. As size filtration experiments indicated and laboratory microcosms showed, endemic V. cholerae could rapidly grow in a free-living state in natural lake water at growth rates similar to those of the bulk natural bacterial population. **Temperature and the quality of dissolved organic carbon had a highly significant influence on V. cholerae growth. Specific growth rates, growth yield, and enzyme activity decreased markedly with increasing concentrations of high-molecular-weight substances, indicating that the humic substances originating from the extensive reed belt in the lake can inhibit V. cholerae growth.**

Vaccine. 2008 Jun 6;26(24):3055-8. Epub 2007 Dec 26.

Genetic diversity-independent neutralization of pandemic viruses (e.g. HIV), potentially pandemic (e.g. H5N1 strain of influenza) and carcinogenic (e.g. HBV and HCV) viruses and possible agents of bioterrorism (variola) by enveloped virus neutralizing compounds (EVNCs).

Kotwal GJ.

Department of Medicine, University of Massachusettes, Worcester, MA 01605, USA.
GJKOTW01@gmail.com

Genetic diversity and hypermutation contribute to difficulties in developing a vaccine against viruses like HIV and influenza. There are currently no known immune correlates of protection against HIV. This has made the development of a vaccine against HIV that would provide sterilizing immunity in the near future an impossible task. The abandonment of a recent AIDS vaccine human trial due to a failure to elicit a protective sterilising immune response confirms that empirical attempts to develop a vaccine may result in failures. Also the difficulty in predicting the next pandemic strain of influenza may make it difficult to respond rapidly should there be an outbreak. Therefore, it is time to explore broad spectrum agents that can target either the lipid portion of the envelope or the sugar moieties of the glycoproteins or the rafts (regions within viral and cell envelopes where a higher concentration of the glycoproteins exist). **Broad spectrum agents that can serve as disrafters or neutralize the viral infectivity by binding to the envelope lipid or sugar moieties will not be affected by the vagaries of hypermutation of surface antigens**. This is because the post-translation modification is a host function. Presented here is a review of recently reported agents present in pomegranate juice (polyphenols, beta-sitosterol, sugars and ellagic acid) and fulvic acid, described here as the envelope virus neutralising compounds (EVNCs) and complex molecules like lectins and mucins. Pomegranate juice was previously reported to inactivate HIV and further shown by our group to inactivate influenza, herpes viruses and poxviruses. **A formulation consisting of fulvic acid, a complex mixture of compounds was previously reported to render vaccinia virus, HIV and SARS virus non-infectious. Recently, both fulvic acid and pomegranate juice have been shown to inactivate genetically diverse strains of influenza including H5N1, further confirming the broad spectrum nature of these agents.** How EVNCs will be used in developing a vaccine achieving sterilizing immunity or prophylaxis needs to be researched.

Biosci Biotechnol Biochem. 2007 May 7; [Epub ahead of print]

Inhibitory Effect of Fulvic Acid Extracted from Canadian Sphagnum Peat on Chemical Mediator Release by RBL-2H3 and KU812 Cells.

- **Yamada P**,
- **Isoda H**,
- **Han JK**,
- **Talorete TP**,
- **Yamaguchi T**,
- **Abe Y**.

Graduate School of Life and Environmental Sciences, University of Tsukuba.

Fulvic acid (FA) was extracted and purified from Canadian Sphagnum peat **(CP-FA)** and characterized by using an element analysis meter, Fourier transform infrared (FT-IR) spectroscopy, electron spin resonance (ESR) spectroscopy, and (13)C-nuclear magnetic resonance ((13)C-NMR) spectroscopy. To investigate the antiallergic effect of CP-FA, we incubated rat basophilic leukemia (RBL-2H3) cells with 0.001-10.0 mug/ml of CP-FA and determined the beta-hexosaminidase release inhibition at different response stages. The intracellular calcium [Ca(2+)](i) level was also determined by using Fluo 3-AM, a calcium-specific fluorescent probe, and the cytotoxicity of CP-FA was determined by the 3-(4,5-dimethythiazol-2-yl)-2,5-diphenyl-tetrazolium bromide (MTT) assay. The results revealed that RBL-2H3 cells incubated for 48 h with 0.001-10.0 mug/ml of CP-FA did not show any decreased viability. **CP-FA inhibited the beta-hexosaminidase release by IgE-sensitized, antigen-stimulated RBL-2H3 cells at the antigen-antibody binding stage and the antibody-receptor binding stage. CP-FA also inhibited histamine release from A23187 plus PMA- or compound 48/80-stimulated KU812 cells. Furthermore, there was a decrease in the intracellular [Ca(2+)](i) level in IgE-sensitized cells incubated with CP-FA and stimulated with antigen. Our results show that CP-FA may be useful for the treatment or prevention of allergic diseases.**

So Light Humics may have antihistaminic properties, although the precise modes of action on this complex process needs more elucidation. A colleague of mine claims that the FA I gave him helped his asthma, however, this is anecdotal.

1: J Anim Sci. 2006 Sep;84(9):2482-90.

Effects of dietary humic substances on pig growth performance, carcass characteristics, and ammonia emission.

- **Ji F**,
- **McGlone JJ**,
- **Kim SW**.

Department of Animal and Food Sciences, Texas Tech University, Lubbock, TX, USA.

Five experiments were conducted to test the effects of various dietary humic substances (HS; HS1, 2, 3, and 4, each with different fulvic and humic acid contents) on pig growth, carcass characteristics, and ammonia emission from manure. In Exp. 1, 120 pigs were allotted to 3 dietary treatments without HS (control) or with HS1 at 0.5 and 1.0% (8 pens/treatment and 5 pigs/pen) and fed diets, based on a 5-phase feeding program, from weaning (d 21.3 +/- 0.3 of age) to 60 kg of BW. In Exp. 2 and 3, 384 pigs (192 for each experiment) were allotted to 3 dietary treatments without HS, with HS1, or with HS2 (0.5%) for Exp. 2 and without HS, or with HS3 or HS4 (0.5%) for Exp. 3 (8 pens/treatment and 8 pigs/pen in each experiment). Pigs were fed diets, based on a 6-phase feeding program, from weaning (25.4 +/-0.2 and 23.6 +/-0.3 d of age for

Exp. 2 and 3, respectively) to 110 kg of BW. In Exp. 4, 96 pigs were weaned at 22.1 +/- 0.2 d of age and allotted to 2 treatments without or with HS1 at 0.5% (6 pens/treatment and 8 pigs/pen), and in Exp. 5 96 pigs were weaned at 20.9 +/-0.3 d of age and allotted to 3 treatments without HS, or with HS3 or HS4 (0.5%; 4 pens/treatment and 8 pigs/pen). Pigs were fed the diets for at least 2 wk before they were moved to an environmental chamber to measure aerial ammonia and hydrogen sulfide for 48 h at 5-min intervals. In Exp. 1, pigs fed diets with HS1 at 0.5% had greater ($P < 0.05$) ADG during phase 3 and greater ($P < 0.05$) G:F during phases 3 and 5 than control pigs. **In Exp. 2, pigs fed diets with HS1 or HS2 at 0.5% had greater ($P < 0.05$) ADG and G:F than control pigs during the entire feeding period, whereas in Exp. 3 HS3 or HS4 did not improve pig growth performance. Ammonia emission from manure was reduced by 18 or 16% when pigs were fed diets with HS1 ($P = 0.067$) or HS4 ($P = 0.054$), respectively. <u>The results of this study indicate that the effects of dietary HS are variable but may improve growth performance of pigs and reduce ammonia emission from manure</u>.**

The mechanism of ammonia sorption by Humic Substances (HS) is as follows….

H-HS + NH_3 → NH_4-HS. The gas is protonated and adsorbed to the HS.

Humic acids reduce the genotoxicity of mitomycin C in the human lymphoblastoid cell line TK6

G. Ferrara[a], E. Loffredo[b], N. Senesi[b] and R. Marcos[c]

Mutation Research/Genetic Toxicology and Environmental Mutagenesis

Volume 603, Issue 1, 31 January 2006, Pages 27-32

Abstract

The antimutagenic/desmutagenic activity of a leonardite humic acid (LHA) and a soil humic acid (SHA) was studied in the cultured human lymphoblastoid cell line TK6 treated with mitomycin C (MMC) as reference mutagen by evaluating the induction of micronuclei (MN). Two different concentrations of HA were used, 2.5 and 10 :g/ml, in three different treatments: (1) HA alone (genotoxic test); (2) HA after 2-h pre-incubation with 0.3 :M of MMC (desmutagenic test) and (3) combinations of HA and MMC at 0.3 :M without pre-incubation (antimutagenic test). Neither of the HA used alone did produce genotoxic effects, but both HAs reduced significantly the frequencies of MN induced by MMC, especially in the desmutagenic test**. A slight cell-protective effect against the cytoxicity of MMC was also exhibited by the two HAs in the desmutagenic test. The LHA showed a desmutagenic/antimutagenic activity that was more pronounced than that of SHA, which is possibly related to the higher carboxylic group content and lower phenolic group content of LHA. These results confirm the antigenotoxic action exerted by HAs in human cells, similarly to what has been previously observed in various plant species.**

Keywords: Humic acids; Mitomycin C; Micronuclei; Human lymphoblastoid cell line; Antimutagenic activity; Desmutagenic activity; Genotoxicity; Cytotoxicity

Corresponding author. Tel.: +39 080 5442491; fax: +39 080 5442976.

1: Clin Ther. 2005 Jun;27(6):755-61.

Prescript-Assist probiotic-prebiotic treatment for irritable bowel syndrome: a methodologically oriented, 2-week, randomized, placebo-controlled, double-blind clinical study.

Bittner AC, **Croffut RM**, **Stranahan MC**.

Battelle Seattle Research Center, Washington, USA. drbittner@comcast.net

BACKGROUND: **The symptomatic efficacy of Prescript-Assist (Safer Medical, Inc., Fort Benton, Montana; Proprietary Blend of Micro-flora and Leonardite 550 mg),** a treatment combining probiotic and prebiotic components, has previously been evaluated clinically only in an open-label study in patients with various gastrointestinal conditions, including irritable bowel syndrome (IBS). OBJECTIVES: This study was conducted primarily to compare the effects of Prescript-Assist with placebo in patients with a diagnosis of IBS. Toward this objective, a secondary methodologic goal was to determine the number and nature of symptom clusters ("subsyndromic factors") that characterize IBS. METHODS: This was a double-blind, placebo-controlled clinical study in which patients were randomly assigned to receive either Prescript-Assist one 500-mg capsule BID or 1 placebo capsule BID for 2 weeks. Thirteen IBS symptoms identified from the clinical literature were embedded in a larger research instrument. Using a scale from 0 to 5, patients rated the intensity of these symptoms for the 7-day period immediately before the start of treatment, at the end of each study week, and after each of the 2 subsequent weeks (during which all patients received open-label Prescript-Assist as part of a larger study evaluating methodologic approaches to enhancing assessments of medication efficacy/safety). The symptom-intensity data were subjected to maximum likelihood factor analysis with varimax rotation to identify any IBS subsyndromic factors, and the effect of treatment on each of the identified factors was evaluated using analyses of covariance with appropriate baseline-week assessments as covariate controls. RESULTS: **The study included 25 patients with IBS (23 women, 2 men; age range, 20-70 years). Three subsyndromic factors were identified that together accounted for 60.2% of total IBS symptom variance: factor 1, general ill feelings/nausea; factor 2, indigestion/flatulence; and factor 3, colitis. Treatment with Prescript-Assist was associated with significant reductions in each of the subsyndromic factors.** Factor 1 was significantly reduced by 0.345 standard score units ($F(1,46) = 4.26$; $P = 0.042$), factor 2 by 0.544 standard score units ($F(1,46) = 7.83$; $P = 0.008$), and factor 3 by 0.826 standard score units ($F(1,46) = 10.20$; $P = 0.003$). CONCLUSIONS: This study identified 3 subsyndromic factors of IBS: general ill feelings/nausea, indigestion/flatulence, and colitis. In this methodologically oriented double-blind study in patients with IBS, combined probiotic-prebiotic treatment with Prescript-Assist was associated with significant reductions in these factors.

The Leonardite in the Prescript-Assist are deposits of oxidized lignite (humate) found in North Dakota

1: Vascul Pharmacol. 2005 Sep;43(3):164-70.

Angiogenesis and cardioprotection after TNFalpha-inducer-Tolpa Peat Preparation treatment in rat's hearts after experimental myocardial infarction in vivo.

Krzemiński TF, **Nozyński JK**, **Grzyb J**, **Porc M**, **Zegleń S**, **Filas V**, **Skopińska-Rózewska E**, **Sommer E**, **Filewska M**.

Department of Pharmacology, Medical University of Silesia, 41-808 Zabrze, Jordana 38, Poland. tadkrzem@ka.onet.pl

The aim of the presented work was to evaluate whether short subcutaneous (s.c.) administration of TNFalpha-inducer-Tolpa Peat Preparation (TPP or TPP batch 0210) modulates the process of ischemic remodeling and spontaneous angiogenesis after experimental myocardial infarction (MI) in rats in vivo. The results obtained using three complementary and correlative methods: histological studies, Proliferating Cell Nuclear Antigen (PCNA) reaction and Lymphocytes Induced Angiogenesis (LIA) test **showed a clear pro-angiogenic and cardioprotective effect of TPP administration after experimental MI. TPP batch 0210 should be considered as an angiogenesis stimulating factor and consecutively as a cardioprotective preventing development of ischemic cardiomyopathy after MI in rats.** It might possibly be used as an adjunct to conventional therapy of coronary artery disease, including late phase after myocardial infarction or ischemic cardiomyopathy.

Tolpa Peat Preparation contains light humics extracted from peat.

PMID: 15269914 [PubMed - indexed for MEDLINE]

1: Poult Sci. 2004 Jan;83(1):84-8.

The effects of supplementation of humate and probiotic on egg production and quality parameters during the late laying period in hens.

- **Yoruk MA**,
- **Gul M**,
- **Hayirli A**,
- **Macit M**.

Department of Animal Nutrition and Nutritional Disorders, School of Veterinary Medicine, Ataturk University, Erzurum 25700, Turkey. mayoruk@hotmail.com

This study was designed to investigate whether inclusions of humate and probiotic into diets of hens during the late laying period increases egg production and improves egg quality. Hisex Brown layers (n = 300), 54 wk of age, were fed a control diet, 0.1% humate, 0.2% humate, 0.1% probiotic, or 0.2% probiotic for 75 d. **Active ingredients of humate and probiotic were polymeric polyhydroxy acids (humic, fulvic, ulmic, and humatomelanic acids)** and bacterial cultures (Lactobacillus, Bifidobacterium, Streptococcus, and Enterococcus spp.), respectively. Egg production and feed intake were measured daily, and egg weight was measured biweekly. Also, a sample of 12 eggs from each group was collected randomly to determine egg quality every 25 d. The data were analyzed as repeated measures with time as subplot. **There were no effects of dietary treatments on feed intake and egg weight**. **Egg production for hens supplemented with humate and probiotic was not different**

but was greater than for control hens. Egg production increased linearly and mortality and feed conversion efficiency (weight of feed/weight of eggs) increased linearly with increasing levels of supplemental humate and probiotic. There were no effects of treatments on egg quality. In conclusion, supplementation of humate and probiotic during the late laying period increased egg production, reduced mortality, and improved feed conversion efficiency but did not improve egg quality.

This study uses raw humate and a humic substances/bacterial culture mix, of which fulvic acid is one component.

PMID: 14761088 [PubMed - indexed for MEDLINE]

Anticlastogenic, antitoxic and sorption effects of humic substances on the mutagen maleic hydrazide tested in leguminous plants

Authors: G. Ferrara[1]; E. Loffredo[1]; N. Senesi[1]
Source: European Journal of Soil Science, Volume 55, Number 3, September 2004, pp. 449-458(10)
Publisher: Blackwell Publishing

Summary
The potential anticlastogenic and antitoxic effects of a soil humic acid (HA), a peat HA and a peat fulvic acid (FA) on the mutagen maleic hydrazide (MH) have been investigated in two legume species, *Vicia faba* and *Pisum sativum*. Both HAs and FA were tested at two different concentrations, 20 and 200 mg l^{-1}, either alone or after 24-hour interaction with 10 mg l^{-1} of MH before addition to the legume seeds. **Anticlastogenicity, i.e. an antimutagenic action defined as the capacity for minimizing chromosome breakages, was evaluated by counting both micronuclei (MN) and aberrant anatelophases (AAT) in root-tip cells**. Length and dry weight of the seedling primary root were measured to test the antitoxic activity of HA and FA on MH. The possible occurrence and extent of adsorption or desorption of MH onto or from HA were also investigated. The two species responded differently to the anticlastogenic tests, with *V. faba* showing a greater number of MN and AAT anomalies than *P. sativum*. **Peat HA and FA exhibited anticlastogenic and antitoxic activities of similar intensity and greater than those of soil HA. The adsorption capacity of both HAs for MH was small, thus suggesting that adsorption is not a major mechanism responsible for the reduction of clastogenicity and antitoxicity of MH by HA.**

1: Life Sci. 2004 Aug 27;75(15):1817-31.

Humic acid induces apoptosis in human premyelocytic leukemia HL-60 cells.

Yang HL, **Hseu YC**, **Hseu YT**, **Lu FJ**, **Lin E**, **Lai JS**.

Institute of Nutrition, China Medical University, Taichung, Taiwan.

It has been shown that humic acid (HA), a phenolic polymer, exhibits pro-oxidant and cytotoxic effects. **In this study, HA induction of apoptosis was studied using cultured human premyelocytic leukemia HL-60 cells. Treatment at a range of HA concentrations (50-400 microg/ml)**

resulted in dose-and time-dependent sequences of events marked by apoptosis, as demonstrated through by apoptotic features such as loss of cell viability, chromatin condensation, and internucleosomal DNA fragmentation. This HA-induced apoptosis in the HL-60 cells was mainly associated with the release of cytochrome c from the mitochondria. Furthermore, apoptosis in the HL-60 cells was accompanied by the activation of caspase-3 and the specific proteolytic cleavage of poly (ADP-ribose) polymerase (PARP), a major component in the apoptotic cell death mechanism. Although the HA-induced apoptosis was associated with Bax protein levels, negligible Bcl-2 reduction was observed. **Analysis of the data reported herein reveals that HA exerts antiproliferative action and growth inhibition on HL-60 cells through induction of apoptosis, which may have anticancer properties potentially useful for the development of new drug products.**

Apoptosis = programmed cell death.

The functions of peritoneal macrophages for the abstract below are delineated in the following study:

Leendertse M, Willems RJ, Giebelen IA, Roelofs JJ, van Rooijen N, Bonten MJ, van der Poll T. 2009. **Peritoneal macrophages are important for the early containment of Enterococcus faecium peritonitis in mice**. *Innate Immun*. 2009 Feb;15(1):3-12.

.....In an ex vivo setting, **peritoneal macrophages** harvested from C57BL/6 mice were responsive to, and **able to phagocytose and kill, E. faecium**. .....This study indicates that peritoneal macrophages are important in the early containment of E. faecium peritonitis and for the regulation of the inflammatory response.

: J Agric Food Chem. 2003 Aug 27;51(18):5245-54.

Characterization and biological activities of humic substances from mumie.

- **Schepetkin IA**,
- **Khlebnikov AI**,
- **Ah SY**,
- **Woo SB**,
- **Jeong CS**,
- **Klubachuk ON**,
- **Kwon BS**.

Immunomodulation Research Center, University of Ulsan, Moo-keo Dong, Nam-ku, Ulsan 680-749, Korea.

Mumie, a semihard black resin formed by long-term humification, is believed to have therapeutic properties. Although mumie has been used in folk medicine since ancient times, there is little information available concerning the physicochemical properties of its constituents and the mechanisms of its therapeutic efficacy. **For this**

study crude mumie was fractionated into fulvic acid (FA), humic acid (HA), humin, hymatomelanic acid, and two low molecular weight fractions (LMW1 and LMW2). The FA fraction was divided into five subfractions, FA1-FA5. The mumie fractions were characterized by IR, UV-vis, and fluorescence spectroscopy. Total carbohydrate content in the fractions was analyzed using the phenol reaction method. The relative content of polar groups and nonpolar hydrocarbon fragments in the mumie fractions correlated well with solubility in an aqueous medium. Biological characterization was performed using only the FA fractions. **FA1 and FA2 enhanced the production of reactive oxygen species (ROS) and nitric oxide in murine peritoneal macrophages**, as determined with the use of 2',7'-dichlorofluorescin diacetate and Griess reagent, respectively. The enchancement of ROS and nitric oxide production correlated with the level of total carbohydrates in the fractions. **Murine splenic lymphocytes treated with FA1 showed a dose-dependent increase in [(3)H]thymidine uptake. These findings suggest that FA derived from mumie has immunomodulatory activity.**

J Hazard Mater. 2003 Jun 27;100(1-3):285-300.

Research Article

Topical application of oxifulvic acid suppresses the cutaneous immune response in mice

Constance E.J. Van Rensburg [1*], Susan C.K. Malfeld [1], Johan Dekker [2]

[1]Medical Research Unit for Inflammation and Immunity, Department of Immunology, Institute for Pathology, Faculty of Medicine, University of Pretoria, South Africa
[2]Enerkom (Pty) Ltd., Pretoria, South Africa

Department of Trade and Industry of South Africa

Keywords

oxifuvic acid; diclofene sodium; betamethasone; topical antiinflammatory; mice

Abstract

The **antiinflammatory activity of topically applied coal-derived fulvic acids** (called oxifulvic acid) at 4.5% and 9% was compared with that of diclofene sodium at 1% and betamethasone at 0.1% in a murine model of contact hypersensitivity. Mice were sensitised with dinitrofluorobenzene and challenged 6 days later by application to the dorsal surface of the right ear. **The inflamed ears of the mice were then treated topically, and the thickness of the ears was measured daily. Oxifulvic acid at both concentrations compared favourably with both diclofene sodium and betamethasone in suppressing the cutaneous inflammatory response. Oxifulvic acid possesses antiinflammatory properties and may be of clinical benefit in the treatment of inflammatory skin conditions in humans.** Drug Dev. Res. 53:29-32, 2001. © 2001 Wiley-Liss, Inc.

1: Z Naturforsch [C]. 2003 Mar-Apr;58(3-4):263-7.

Investigation of the immunostimulatory properties of oxihumate.

Jooné GK, **Dekker J**, **van Rensburg CE**.

Department of Pharmacology, Faculty of Medical Sciences, University of Pretoria, PO Box 2034, Pretoria, 0001, South Africa. cmedlen@postillion.up.ac.za

A unique process has been developed to convert bituminous coal by controlled wet oxidation followed by base treatment to a water-soluble humate called oxihumate. **The effects of oxihumate on the proliferative response of lymphocytes has been studied in vitro and ex vivo. Oxihumate increased the proliferative response of phytohaemagglutinin-stimulated human lymphocytes, from a concentration of 20 microg/ml and upwards. This response was even more striking in the case of lymphocytes from HIV-infected patients and was not limited to the in vitro setting since similar effects were observed ex vivo following administration of a non-toxic dosage of 4 g oxihumate per day to HIV-positive individuals for two weeks. Mechanistic studies revealed that stimulation of the proliferative response of lymphocytes by oxihumate 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. Oxihumate therefore holds promise for the treatment of immunocompromized patients.**

PMID: 12710739 [PubMed - indexed for MEDLINE]

1: Int J Pharm. 2003 Mar 6;253(1-2):169-75.

Evaluation of the permeation of peat substances through human skin in vitro.

- **Beer AM**,
- **Junginger HE**,
- **Lukanov J**,
- **Sagorchev P**.

Department Naturopathy, Blankenstein Hospital, Hattingen, Germany.

Peat and various peat extracts have been successfully applied for a variety of clinical indications. Quite apart from the physico-thermal effects, **new studies point towards the so-called "chemical effects" of peat containing substances. These effects include a stimulatory response of the spontaneous contractile activity (SCA) of smooth muscle (SM) tissue. The effects are, however, dependent on the possible permeability of pharmacologically active substances as naturally occurring ingredients of peat.** Since peat is a mixture of various products it is necessary to examine the various peat types based upon their biological activity on SM tissue. In order to unequivocally prove the pharmacological activity of cutaneous peat treatment, in vitro permeation measurements of these actives across excised human skin can be used.HPLC analysis revealed that aqueous peat extracts contain up to 18 fractions of water-soluble compounds of fulvic and ulmic acids. **These compounds**

have been found to have a stimulatory response on the contractile activity of SM tissue. In vitro diffusion studies showed that the permeability of these substances across human full thickness skin (thickness: 200 um(-1)) is highly selective and the resulting stimulatory activity is dependent on the permeated fraction. Especially, the HPLC fractions 7-11 and 14 are able to permeate human skin. Fractions 7-11 show a moderate stimulatory effect of SCA on SM for more than 90 min whereas fraction 14 shows the strongest stimulatory effect which was, however, suppressed after 87 min. **These results show that the cutaneous therapy with peat treatment results in transcutaneaous permeation of biologically active fulvic and ulmic acid derivatives explaining the additional "chemical" effect of peat treatment in clinical practice.**

PMID: 12593947 [PubMed - indexed for MEDLINE]

Schepetkin, Igor, Andrei Khlebnikov and Byoung Se Kwon. 2002. **Medical drugs from humus matter: Focus on mumie.** *Drug Development Research*, Drug Development Research 57, 3, 140--159

Abstract

In this review, we focus on the medicinal drugs from humus matter such as peat, sapropel, and mumie. The most clinically available medicines, containing peat and sapropel extracts, are Torfot, Tolpa Peat Preparation (TPP), Peloidodistillate, Humisol, Peloidin, FiBS, and Eplir. Much attention in the review is concentrated on mumie composition, its pharmacological properties, and new pharmacological drugs with mumie (Shilagen, Abana, Cystone, Diabecon 400, EveCare, Geriforte, Lukol, Pilex, Rumalava, Tentex forte, Nefrotec, Adrenotone, Siotone, La-Tone Gold, Andro-Surge, Solanova Libidoplex). **It was concluded that therapeutic properties of crude extracts from peat, sapropel, and mumie have similarity to the ones of fulvic and humic acids. They are antibacterial, antitoxic, antiradical, antiulcerogenic, antiarthritic, immunomodulatory, and antiinflammatory properties.** Possible directions for better development of new drugs from humus matter are discussed.

English Keywords

Toxicity ; Ion transport ; Radical scavenger ; Free radical ; Antiinflammatory agent ; Immunomodulator ; Antiulcer agent ; Antibacterial agent ; Antioxidant ; Biological activity ; Humic acid ; Fulvic acid ; Pharmacognosy ; Humification ; Peat ; Review ; Plant origin ; Humus ;

1: Poult Sci. 2002 Feb;81(2):227-30.

The effects of dietary humate supplementation on broiler growth and carcass yield.

- Kocabagli N,
- Alp M,
- Acar N,
- Kahraman R.

Department of Animal Nutrition and Nutritional Diseases, Faculty of Veterinary Medicine, University of Istanbul, Avcilar, Turkey. kbagli@istanbul.edu.tr

The growth-promoting effect of Farmagulator DRY Humate (FH) on live performance, carcass weight, and the abdominal fat pad of broilers was studied during different feeding periods. Four hundred, 1-d-old straight-run birds were randomly distributed to 20 floor pens of an environmentally controlled house. Four dietary regimens were replicated in five pens, each containing 20 chicks, as follows: 1) birds received no added FH in the starter or grower (NAFH), 2) birds received FH from 0 to 21 d (FH0-21), 3) birds received FH from 22 to 42 d (FH22-42), 4) birds received FH from 0 to 42 d (FH0-42) in the starter and grower diets, respectively. The FH was added to the diets at 2.5 kg/per ton of feed. Starter and grower diets were formulated to meet the minimum NRC requirements for broilers and were provided as a mash feed. Body weights at 21 d were not affected by the dietary regimens. **At 42 d, body weights and feed conversions of broilers were significantly affected by the dietary humate treatments. Birds fed FH22-42 weighed more than the NAFH, whereas the FH0-21 and FH0-42 were intermediate and not different from the other treatments. Feed:gain was lower for the FH22-42 and FH0-42 treatments compared to the NAFH. There was no difference in carcass yield or abdominal fat pad percentages due to feeding FH. Feeding FH during the grower period had the most beneficial effect in terms of growth and feed conversion on broiler performance.**

PMID: 11873831 [PubMed - indexed for MEDLINE]

1: Clin Ter. 2001 Nov-Dec;152(6):347-51.

Effect of water of Anticolana Valley on urinary sediment of renal stone formers.

- Fraioli A,
- De Angelis Curtis S,
- Ricciuti G,
- Serio A,
- D'Ascenzo G.

Department of Medical Therapy, University of Rome La Sapienza, Rome, Italy.

An investigation was carried out to ascertain the effect of drinking Fiuggi water on the microcrystalline structure of the calcium oxalate monohydrate present in urinary sediments provided from patients suffering from recurrent idiopathic

oxalic calculosis. The experimental group was administered tap and Fiuggi water for ten days. The control group was administered tap and Fiuggi water according to the same procedure as for the experimental group. **The comparative data show that drinking Fiuggi water leads to a strong reduction, and sometimes even to the elimination, of the calcium oxalate monohydrate present in the urinary sediment reducing the risk of oxalic calculosis. Fiuggi water contains organic molecules belonging to the fulvic acid family. These acids are capable of complexing the calcium ions and interact preferentially with the crystal lattice of the calcium oxalate monohydrate via the formation of a film and behave as pumping systems by linking the calcium ion, demolishing the crystal lattice and dissolving calcium and oxalate ions.** Mineral water treatments must therefore be viewed as a function of the specific composition of the water administered. The ecosystem influences the composition of water, as a complex matrix containing a number of organic molecules which are potentially biologically active.

PMID: 11865529 [PubMed - indexed for MEDLINE]

1: Environ Sci Technol. 2001 Oct 1;35(19):3841-8.

Quantification and prediction of the detoxifying properties of humic substances related to their chemical binding to polycyclic aromatic hydrocarbons.

- **Perminova IV**,
- **Grechishcheva NY**,
- **Kovalevskii DV**,
- **Kudryavtsev AV**,
- **Petrosyan VS**,
- **Matorin DN**.

Department of Chemistry, Lomonosov Moscow State University, Russia. iperm@cityline.ru

Effects of 27 different humic materials on the toxicity of polycyclic aromatic hydrocarbons (PAH) were studied for crustacean Daphnia magna. Sources included isolated humic acids, fulvic acids, and their combination from soil, peat, and freshwater. The PAH used were pyrene, fluoranthene, and anthracene. **The observed reduction in toxicity of PAH in the presence of humic substances (HS) was shown to be a result of the detoxification effect caused by the chemical binding of PAH to HS and of the direct effect of HS on D. magna. An approach was developed to quantify the detoxifying impact of humic materials related to their chemical binding to PAH with a use of the "constant of detoxification" or "toxicological partition coefficient" K(oc)D**. The latter was proposed to determine by fitting the experimental relationships of the detoxification effect versus concentration of HS. The obtained K(oc)D values were well tracked by the corresponding partition coefficients determined by the fluorescence quenching technique (K(oc)fq): K(oc)D=b x K(oc)fq, b (mean+/-Cl, n=26, P=95%)=2.6+/-0.3, 4.6+/-0.6, and 6.0+/-1.4 for pyrene, fluoranthene, and anthracene, respectively. The predictive relationships

between the structure and detoxifying properties of humic materials in relation to PAH were developed. It was shown that the magnitude of the K(oc)D values correlated closely with the aromaticity of humic materials characterized with the 13C NMR descriptors (sigma(C)Ar, sigma(C)Ar/sigma(C)Alk) and atomic H/C ratio. The obtained relationships showed the highest detoxifying potential of the humic materials enriched with aromatics and allowed a conclusion on the chemical binding as the governing mechanism of the mitigating action of HS on the toxicity of PAH.

PMID: 11642442 [PubMed - indexed for MEDLINE]

1: Phytomedicine. 2000 Oct;7(5):407-15.

The influence of fulvic and ulmic acids from peat, on the spontaneous contractile activity of smooth muscles.

- **Beer AM**,
- **Lukanov J**,
- **Sagorchev P**.

Department of True naturopathy, Blankenstein Hospital, Hattingen, Germany.

The aim of the presented studies was to evaluate which classes of compounds of peat ingredients could be responsible for the partial agonistic effect of aqueous peat extract on the alpha2 adreno and D2 dopamine receptors of smooth muscles, which we have reported from former investigations. Based on the different solubility of peat ingredients, water-soluble components of fulvic and ulmic acids were separated according to the pH-value and chemical structure of the solvent. The biological activity of these acids was examined in peat baths using smooth muscle fibers of guinea pig stomach. **The results demonstrate that the water-soluble components of fulvic and ulmic acids have a partially agonistic effect on the alpha2 adreno and D2 dopamine receptors, but at the same time quite different effects in terms of their influence on the spontaneous contractile activity (SCA) of smooth muscles have to be noted.** From these investigations, we can conclude that aqueous peat extract and the water-soluble components of fulvic acid exhibit similar partial agonistic effects on the alpha2 adreno and D2 dopamine receptors. Therefore it is likely that the mentioned effects of the peat extract derive from the fulvic- and ulmic acids only. The water-soluble component of ulmic acid also showed partial agonistic effects on alpha2 adreno and D2 dopamine receptors. In this case, another substance group is involved, which has a faster blocking effect on these receptors, but was barely soluble in water at a normal pH-value (pH 7).

an agonist is a substance that binds to a specific receptor and triggers a response in the cell. In humans dopamine inhibits motility in the upper gut, but stimulates motility in the colon ~ reduces cramping in the upper gut.

Acta Pol Pharm. 2000 Nov;57 Suppl:127-9

The research on antioxidative properties of TOŁPA Peat Preparation and its fractions.

Piotrowska D, **Długosz A**, **Witkiewicz K**, **Pajak J**.

Department of Toxycology, Wroclaw Medical University, 57/59 Traugutta Str., Wroclaw.

The protective and therapeutic role of TPP and its fractions against lipid peroxidation in the mitochondria from human placenta as a model for experiments was evaluated. **Both TPP and its fractions cause the decrease in MDA production. The antioxidant force of TPP and its fractions with antioxidant force of vitamin E was compared.**

J Antimicrob Chemother. 2000 Nov;46(5):853.

An in vitro investigation of the antimicrobial activity of oxifulvic acid.

- **van Rensburg CE**,
- **van Straten A**,
- **Dekker J**.

Humic substances, of which 90–95% are fulvic acids, commonly account for 50% of the dissolved organic carbon in stream water..... A South African company [Enerkom (Pty) Ltd] has developed a unique process to convert bituminous coal by controlled wet oxidation with oxygen in high yield to high quality humic and fulvic acids. To distinguish these coal-derived products from naturally occurring humic and fulvic acids, the former are called oxihumic and oxifulvic acid respectively. .....The effect of oxifulvic acid solutions on the growth of eight microbial pathogens was determined by the macrobroth tube dilution method.[4] Oxifulvic acid, supplied by Enerkom (Pty) Ltd, was dissolved in water to a concentration of 240 g/L and further diluted in brain heart infusion broth. **All eight organisms tested were sensitive to oxifulvic acid at a concentration of 15 g/L (Table⇔), *Enterococcus faecalis* and *Klebsiella pneumoniae* being susceptible to concentrations as low as 5 g/L.**

It has been demonstrated in two pilot studies that oxifulvic acid is effective in the topical treatment of pyotraumatic dermatitis in cats and dogs[5] and also inhibits contact hypersensitivity in mice. Oxifulvic acid did not produce any measurable toxicity in experimental animals during either acute or sub-chronic dermal exposure to 5.3% oxifulvic acid cream (results not shown). The antimicrobial properties, together with its anti-inflammatory properties, suggest that oxifulvic acid, applied topically, might be an effective and safe treatment for skin infections.

Zhongguo Zhong Yao Za Zhi. 1997 Sep;22(9):559-61 inside back cover.

[Inhibition of hydrogen peroxide production on chondrocytes induced by fulvic acid by ginger volatile oil]

[Article in Chinese]

- **Guo P**,
- **Xu J**,
- **Xu S**,
- **Wang K**.

School of Pharmaceutical Sciences, Beijing Medical University.

In order to investigate the effect of ginger on Kashin-Beck disease (KBD), the ginger volatile oil was taken as a scavenger and proved effective in inhibiting the production of hydrogen peroxide in chondrocytes induced by fulvic acid from KBD area.

PMID: 11038952 [PubMed - indexed for MEDLINE]

Time to add ginger to selenium as cofactors to be taken with fulvic acid as a preventative of Kashin-Beck disease; which is caused by selenium deficiency and appears to be exacerbated by fulvic acid.

1: J Antibiot (Tokyo). 1999 Jul;52(7):628-34

Mode of action of anhydrofulvic acid against Candida utilis ATCC 42402 under acidic condition.

- **Fujita K**,
- **Nagamine Y**,
- **Ping X**,
- **Taniguchi M**.

Department of Bio- and Geoscience, Graduate School of Science, Osaka City University, Osaka, Japan.

The mode of action of **anhydrofulvic acid against the yeast Candida utilis** ATCC 42402 was **investigated under acidic conditions**. Anhydrofulvic acid inhibited the incorporation of radioactive precursors into DNA, RNA, protein and lipid fractions. Although it did not induce leakage of intracellular materials from the treated cells, it had

inhibitory effects on both endogenous and exogenous cellular respiration. **Moreover, it inhibited mitochondrial respiration of Candida utilis ATCC 42402 using both succinate and cytochrome c as respiratory substrates, but not using NADH.** Unexpectedly, the inhibition against isolated mitochondria was observed at pH 7.0. These results suggested that the action site against the respiratory inhibition of anhydrofulvic acid might be involved in succinate dehydrogenase, complex II in the mitochondrial electron transport chain of the yeast cells. **Judging from the inhibitory effect of anhydrofulvic acid on mitochondria detected at pH 7.0, it was postulated that the antifungal activity at a low pH level might depend on the elevation of drug permeability to the cell membrane under acidic conditions.**

1: Nephron. 1999;81 Suppl 1:98-102.

Solvent effect in vitro of Anticolana Valley water on renal stones: analytical-instrumental study.

- **De Angelis Curtis S**,
- **Curini R**,
- **Fraioli A**,
- **Petronio BM**,
- **Ricciuti G**,
- **D'Ascenzo G**.

Department of Chemistry, University of Rome La Sapienza, Rome (Italy).

The presence of humic and fulvic acids in the Anticolana Valley (Fiuggi) water has been established. On the basis of this evidence we investigated the capacity of Anticolana Valley (Fiuggi) water to dissolve renal calculi in vitro. Crystals of calcium oxalate monohydrate to simulate a kidney stone were prepared. Human renal stones of calcium oxalate monohydrate were obtained by courtesy of the Division of Urology of 'La Sapienza' University (Rome), the Division of Urology of the University of Havana (Cuba) and the ASTIF of Fiuggi. The study was performed using the Anticolana Valley (Fiuggi) water, distilled water and tap water (ACEA, Rome), in a specially designed Perspex apparatus. Each calculus was subjected to a water flow of 2 liters/24 h. **The capacity of the Anticolana Valley (Fiuggi) water to dissolve human and synthetic calculi was found to be much higher than that of distilled water which in turn was significantly more effective than tap (ACEA) water.**

PMID: 9873221 [PubMed - indexed for MEDLINE]

1: Nephron. 1999;81 Suppl 1:93-7.

Chemical analysis of water of the Anticolana Valley: isolation of humic compounds.

- **Calace N**,
- **D'Ascenzo G**,

- **De Angelis Curtis S**,
- **Delfini M**,
- **Fraioli A**,
- **Petronio BM**.

Department of Chemistry, University of Rome La Sapienza, Rome, Italy.

The purpose of this study was to identify and characterize humic compounds in Anticolana Valley (Fiuggi) water. The capacity of this class of compounds to mobilize metals from solid phases could have an important role in calculi solubilization. Humic compounds were isolated, purified and characterised by FTIR, 1H-NMR and 13C-NMR spectroscopy, thermogravimetry and elemental analysis. **Only fulvic acids were found.** They are mainly composed of aliphatic chains, made of six -CH2O- groups and contain a number of carboxylic groups, responsible for their metal complexing capacity.

PMID: 9873220 [PubMed - indexed for MEDLINE]

1: Experientia. 1994 Jun 15;50(6):530-5

The biochemistry of ancient DNA in bone.

- **Tuross N**.

Conservation Analytical Laboratory, Smithsonian Institution, Washington District of Columbia 20560.

The amount of DNA in ancient bone was determined by ethidium bromide staining after the removal of the potent Taq inhibitor, fulvic acid. A complete decalcification and a perfusion protocol were used to recover DNA from bone. A variety of purification techniques including molecular sieve, hydroxyapatite binding and 'Magic' preparations yielded DNA that spanned from 3.4 micrograms/g of bone to below detectable limits**. Fulvic acid was shown to interfere with the quantification of DNA derived from ancient human skeletal material one hundred to over seven thousand years old.** Scanning UV in the 300 to 230 nm range is a simple and sensitive technique for documenting fulvic acid contamination in ancient bone extracts.

In past times, meat was forage fed and grains were grown on the more productive soils – this means, before the advent of chemical fertilizers, that high-organic matter soils were the most productive. In fact, when the "fertility" declined, it was most often due to organic matter depletion, either by erosion or by the oxidation of organic matter (thus releasing nutrients to grow plants). Soils high in organic matter are also relatively high in humic substances. Since lightweight humic substances are absorbed and translocated through the plant, ancient peoples generally had higher levels of fulvic acid in their diet than we do today in our organic-

matter depleted, chemically grown crops, and in the feed from these soils that we give to our animals.

Am J Physiol. 1994 Apr;266(4 Pt 1):L382-8. Links

1: Environ Mol Mutagen. 1993;21(3):237-46.

Formation and characterization of bacterial mutagens from reaction of the alternative disinfectant monochloramine with model aqueous solutions of fulvic acid.

- **Cozzie DA**,
- **Kanniganti R**,
- **Charles MJ**,
- **Johnson JD**,
- **Ball LM**.

Department of Environmental Sciences and Engineering, University of North Carolina, Chapel Hill 27599-7400.

Monochloramine has been suggested as an alternative disinfectant to chlorine to reduce levels of trihalomethanes in treated drinking water, but little is known of the toxicological properties and potential health implications of by-products specific to the chloramination process. **Model aqueous fulvic acid solutions (200-400 mg C/liter), serving as surrogates for humic surface waters, were chloraminated over a range of molar Cl:C ratios from 1:40 to 1:2.** The resulting by-products were extracted into diethyl ether at pH 2 and investigated with the Ames plate incorporation assay. **Extractable mutagenicity increased with increasing chlorine and carbon dose up to about 30,000 revertants/liter at Cl:C ratios of 1:2.** Mutagenicity was higher in Salmonella typhimurium strain TA100 than in strain TA98, and was decreased in the presence of S9, indicating that the mutagens formed were direct-acting and induced predominantly base-pair substitutions. Bovine serum albumin decreased slightly, and glutathione reduced greatly, the mutagenic activity detected in extracts. **HPLC fractionation of the by-products indicated that most of the mutagenic activity was found in the earliest-eluting (most polar) fraction (that's the fulvic acid)**. The mutagenic by-products appeared to be qualitatively similar to 3-chloro-4-dichloromethyl-5-hydroxy-2-(5H)-furanone (MX) in their chromatographic behavior and responses to glutathione and bovine serum albumin, but were less readily detoxified by S9 than was MX.

Take home message – to not use freshly chlorinated water to dilute CXC, due to the formation of polycyclic chlorinated hydrocarbons between the FA and the chlorine. Allow the water to stand for a couple of hours, or use a chlorine free water source.

Arch Immunol Ther Exp (Warsz). 1993;41(1):73-80.

Tołpa Torf Preparation (TTP) induces interferon and tumor necrosis factor production in human peripheral blood leukocytes.

Inglot AD, Zielińska-Jenczylik J, Piasecki E.

Laboratory of Virology, Institute of Immunology and Experimental Therapy, Polish Academy of Sciences, Wrocław.

Abstract

Tołpa Torf Preparation (TTP) is a natural immunomodulating drug registered in Poland for use in humans. **TTP is a biologically active low molecular weight fraction of an extract from peat containing organic substances**, primary bound sugars, amino-acids, **uronic and huminic acids** and mineral salts. The toxicity of TTP is remarkably low, eg. cytotoxicity (CD50) for human peripheral blood leukocytes (PBL) is 1-9 mg/ml. **We have discovered that TTP is an interferon (IFN) and tumor necrosis factor (TNF) inducer in human PBL.** The IFN and TNF response of the PBL cultures was dose dependent. The optimal concentration of TTP for IFN or TNF response was 10-100 micrograms/ml. The cytokines stimulated by TTP were IFN-gamma, IFN-alpha and TNF-alpha. Ten commercial batches of TTP have been found to be active as cytokines inducers although variations in their activities were observed. On the other hand, 8 batches of TTP rejected by the producer because of the inadequate immunostimulating activity determined in mice, were found to be significantly less active than the commercial preparations. Over 115 buffy coats from the individual blood donors were used to prepare PBL cultures for this study. Approximately 20% of the PBL cultures were unresponsive to TTP. The IFN and TNF response of PBL to other inducers: phytohemagglutinin (PHA) or lipopolysaccharides (LPS) also varied. Whereas only 7% of PBL could not be stimulated by PHA, as much as 20-50% of PBL failed to produce IFN or TNF when treated with LPS. **We suggest that TTP may have clinically useful activities connected with the capacity of stimulation of IFNs and TNF production.**

Arch Immunol Ther Exp (Warsz). 1993;41(1):99-103.Links

A comparison of efficacy of Tołpa Torf Preparation (TTP) in the treatment of cervicitis with or without surgery.

Woytoń J, Gabryś M, Bielanów T, Zimmer M, Sokalski J, Geneja R, Zborowski M.

II Department of Obstetrics, Medical Academy, Wrocław, Poland.

Tołpa Torf Preparation (TTP) is an immunomodulating drug produced by Torf Corporation, Wrocław and registered for human use in Poland. **TTP enhances the process of tissue regeneration. Authors evaluate TTP effectiveness in the treatment of inflammatory states of the cervix, especially cervical erosions and the influence of this preparation of the macroscopic, cytological and bacteriological state of the cervix**. TTP was used in 31 patients with the diagnosis of cervical erosion. All patients treated as yet were classified into 3 groups, depending on the treatment of cervical erosion used previously. TTP was administered orally in the dose of 5 mg (in 10 ml of water) daily during 10 days and locally in the form of tampons soaked with 1% TTP solution in the volume of 5 ml also during 10 days. **TTP administered this way has beneficial therapeutic effects on the healing of cervical erosion accelerating the process of epithelialization and bringing normalization of the cytological picture. Especially beneficial in the treatment of cervical erosion is combined use of TTP and electrocoagulation or curettage--the healing time can be shortened by half.**
Arch Immunol Ther Exp (Warsz). 1993;41(1):95-7.Links

A randomised, double-blind study on the efficacy of Tołpa Torf Preparation (TTP) in the treatment of recurrent respiratory tract infections.

Jankowski A, Nienartowicz B, Polańska B, Lewandowicz-Uszyńska A.

TTP is a new immunomodulating drug of natural origin, registered in Poland for human use. In the randomised, double blind study to assess the therapeutic efficacy of the Tołpa Torf Preparation (TTP) in the **recurrent respiratory tract infectious** participated 39 young patients (age 16-22). TTP was administered orally, 5 mg daily for three weeks. During 3 months follow-up period favourable results of treatment were obtained in 14 of 20 TTP treated patients and in 8 of 19 of the placebo patients. The therapeutic effects were seen even after the 6 months follow-up period. The phagocytic activity of granulocytes was significantly stimulated in the TTP--treated patients but not in the placebo-treated patients. **The results suggest that TTP is effective drug in the treatment of recurrent respiratory tract infections with undefined infectious etiology. In the period of the treatment as well as during 6 months observation no side effects were noticed.**

Acta Pol Pharm. 1993;50(4-5):393-5.Links
Influence of Tołpa Peat Preparation on the phagocytic activity and bactericidal properties of granulocytes in healthy volunteers.
Kowalska M, Denys A, Białek J.
Department of Medical Microbiology, Military Medical Academy, Lódź, Poland.

It was found, that Tołpa Peat Preparation (TPP) administered to healthy volunteers in doses of 100-300 mg/day during 14 days evoked the stimulation of the phagocytic and bactericidal activity of the granulocytes. The dose of 600

mg/day causes only a transient and insignificant increase of phagocytic and bactericidal properties of the granulocytes.

1: Biochem J. 1993 Feb 1;289 (Pt 3):829-35.

Fulvic acid supplementation and selenium deficiency disturb the structural integrity of mouse skeletal tissue. An animal model to study the molecular defects of Kashin-Beck disease.

- **Yang C**,
- **Niu C**,
- **Bodo M**,
- **Gabriel E**,
- **Notbohm H**,
- **Wolf E**,
- **Muller PK**.

Institute of Medical Molecular Biology, Medical University of Lubeck, Germany.

High concentrations of fulvic acid and selenium deficiency are the main causative factors of Kashin-Beck disease, an endemic, chronic and degenerative osteoarticular disorder found in China. In the search for an animal model of this disease, mice were exposed to these pathogenetic conditions for two generations and the collagen types from skin, bone and cartilage were analysed. The growth of the treated mice was slightly retarded, and the rate of reproduction was lower in animals maintained on a fulvic acid-supplemented and/or selenium-deficient diet. Irregular bone formation was seen by radiography and morphometry. **Biochemical analysis indicated that lysine residues in collagen I from bone and in collagen II from cartilage were overmodified.** The values of Hyl/(Hyl+Lys) in bone collagen alpha 1(I) chains from treated mice were about 0.434-0.484, i.e. substantially higher than that of the control (0.277). The values of this parameter for collagen II were 0.482 for control and 0.546-0.566 for treated mice. The melting temperature of collagen I from bones of treated mice was 1 degrees C lower than that of control collagen, indicating decreased thermal stability. **The breakage point of the tibiae of treated mice occurred at a lower preload force than for controls, suggesting that the overmodified and thermally less stable collagen molecules are causally related to a lower mechanical strength of bones.**

To preclude any aggravation Light Humics may cause to Kashin-Beck disorder, we need to add selenium (preventative) and ginger (prescriptive) to any Light Humics meant for human consumption.

1: Am Rev Respir Dis. 1992 Feb;145(2 Pt 1):271-5. Links

Arch Orthop Trauma Surg. 1992;111(5):259-64.Links

Collagen stabilization induced by natural humic substances.

Riede UN, Jonas I, Kirn B, Usener UH, Kreutz W, Schlickewey W.

Department of Pathology, Medical School, University of Freiburg, Federal Republic of Germany.

Humic substances are polyphenolic compounds. **They have antiviral as well as desmutagenic effects and react with biopolymers such as collagen; thereby they have no toxic side effects by oral administration. In vitro incubation with humic substances raises the breaking point of the tail tendon of the rat by about 75%. The chemical resistance of the collagen fibres in tail tendon collagen is also increased by in vitro incubation with humic substances**, at least insofar as the ultrastructurally and biophysically measurable destruction of the collagen fibres by 4 M guanidinium chloride is inhibited. As humic substances increase the mechanical and chemical resistance of collagen fibres and promote their "maturity", it seems likely that this effect of humic substances depends upon their interaction with the hydrogen bonding and covalent bonding of the collagen fibres. Such a conclusion is confirmed by the results of X-ray diffraction analysis.

1: Sci Total Environ. 1987 Apr;62:347-54.

Effect of humic substances on mitochondrial respiration and oxidative phosphorylation.

· **Visser SA**.

Fulvic and humic acids extracted from a podzol were shown to stimulate respiration in rat liver mitochondria, when present at concentrations of between 40 and 360 mg L-1. **Low molecular weight fractions induced a more significant increase in respiration than high molecular weight material. Humic substances, at concentrations of between 40 and 400 mg L-1, normally also increased the efficiency of the process of oxidative phosphorylation in vitro**, particularly after contact periods with the mitochondria of over 1 hour.

Excellent article showing that Light Humics are most effective in stimulating respiration efficiency in rat liver mitochondria.

1: Mutat Res. 1987 Feb;176(2):199-204.

Mechanism of the desmutagenic effect of humic acid.

- **Sato T**,
- **Ose Y**,
- **Nagase H**,
- **Hayase K**.

The mechanism of an apparent desmutagenic effect of humic acid was investigated. Firstly, components of humic acid (resorcinol, vanillin, vanillic acid, ferulic acid, protochatechuic acid and benzoic acid) were tested and were not found to show a desmutagenic effect. By contrast, lignin did show a desmutagenic effect. **The desmutagenic effect of humic acid was decreased by ozone treatment, and the degree of decrease corresponded with a decrease in KMnO4 consumption**. Benzo[a]pyrene and humic acid were incubated at 37 degrees C for 1 h and extracted by ethyl acetate and the extract was investigated by gas chromatography (GC). The peak of the decomposition product did not appear, but the amount of benzo[a]pyrene was decreased. **This suggests that the desmutagenic effect of humic acid was caused by adsorption of benzo[a]pyrene by humic acid rather than by decomposition of benzo[a]pyrene**. Humic acid had the largest adsorption activity at its critical micelle concentration (CMC), while adsorbed benzo[a]pyrene could be released by ultrasonication. **Fulvic acid and water-soluble humic substance showed a slight inhibitory effect on the mutagenicity of benzo[a]pyrene.**

Ozone treatment degrades humic substances. This article shows that anti-mutagenic effect of humic acid on benzo(a) pyrene is by sequestration rather than deactivation or direct decomposition. Benzo(a)pyrene is more fat-soluble, and larger humic molecules have more hydrophobic zones for sequestration . Hence, the poorer performance of fulvic acid .

1: Environ Health Perspect. 1986 Nov;69:101-7.

Mutagenic by-products from chlorination of humic acid.

- **Meier JR**,
- **Ringhand HP**,
- **Coleman WE**,
- **Schenck KM**,
- **Munch JW**,
- **Streicher RP**,
- **Kaylor WH**,
- **Kopfler FC**.

Chlorination of humic and fulvic acid results in the formation of direct-acting mutagenicity, detectable in the Salmonella/microsome assay (Ames test). This mutagenicity is being characterized as part of an overall effort aimed at evaluating potential health risks associated with the presence of mutagenic chemicals in drinking water. **A number of chlorinated organic compounds, including several known mutagens, have been identified and quantified in diethyl ether extracts of chlorinated humic acid solutions. However, the total mutagenicity of these compounds accounts for only about 7% of the original mutagenicity. Synergistic or antagonistic interactions among the identified components have**

been ruled out as possible explanations for the failure to account for a higher percentage of the activity. Recent progress has been made to separate the activity into neutral and strong acid fractions. Further isolation of the strong acids by high-pressure liquid chromatography (HPLC) has resulted in the purification of the mutagenicity into a major peak of activity with a specific mutagenicity of about 20,000 TA100 revertants per milligram. Several trichlorohydroxyfuranone isomers have been tentatively identified in this fraction. The contribution of these types of compounds to the mutagenicity of chlorinated humic acid is under investigation.

Although mutagens are formed by the chlorination of HA, the mutagenic activity is only 7% of what is expected. Perhaps chlorinated humic substances show less mutagenicity than other chlorinated hydrocarbons in drinking water.

1: Vopr Kurortol Fizioter Lech Fiz Kult. 1986 Sep-Oct;(5):29-32. Links

[Effect of the humic and fulvic acids of sapropel on the NAD.H-oxidase activity of the liver mitochondria]

[Article in Russian]

- **Ioshchenko SE**.

PMID: 2949424 [PubMed - indexed for MEDLINE]

Abstract not available. If a positive effect was the result, then FA may help speed the rate at which the liver decomposes compounds, including toxins.

Environ Health Perspect. 1982 Dec;46:215-27.

Use of biological assay systems to assess the relative carcinogenic hazards of disinfection by-products.

- **Bull RJ**,
- **Robinson M**,
- **Meier JR**,
- **Stober J**.

Other workers have clearly shown that most, if not all, drinking water in the U.S. contains chemicals that possess mutagenic and/or carcinogenic activity by using bacterial and in vitro methods. In the present work, increased numbers of tumors were observed with samples of organic material isolated from 5 U.S. cities administered as tumor initiators in mouse skin initiation/promotion studies. Only in one case was the

result significantly different from control. In studies designed to test whether disinfection practice contributes significantly to the tumor initiating activity found in drinking water mixed results have been obtained. In one experiment, water disinfected by chlorination, ozonation or combined chlorine resulted in a significantly greater number of papillomas when compared to nondisinfected water. In two subsequent experiments, where water was obtained from the Ohio River at different times of the year, no evidence of increased initiating activity was observed with any disinfectant. Analysis of water obtained at the comparable times of the year for total organic halogen, and trihalomethane formation revealed a substantial variation in the formation of these products. Considering the problems such variability poses for estimating risks associated with disinfection by-products, a model system which makes use of commercially obtained humic acid as a substrate for chlorination was investigated using the ***Ames test.*** **Humic and fulvic acids obtained from two surface waters as well as the commercially obtained humic acid were without activity in TA 1535, TA 1537, TA 1538, TA 98 or TA 100 strains of S. typhimurium. Following treatment with a 0.8 molar ratio of chlorine (based on carbon) significant mutagenic activity was observed with all humic and fulvic acid samples.** Comparisons of the specific mutagenic activity of the chlorinated products suggests that the commercial material might provide a useful model for studying health hazards associated with disinfection reactions by-products.

This has been a hazard even in wastewater that is initially low in humic substances, because during the microbial decomposition process on the sewage, a small amount of humic substances are produced. The mutagenicity of chlorinated wastewater can be substantial. It remains a hazard that speaks against the chlorination of water. Ozonation is much better as carbon dioxide and water are the decomposition products with no residual disinfection effect. Ozonation is more expensive, so it hasn't been widely adopted.

Generally it is probably wise to use non-chlorinated liquids as a diluent for light humics, or let chlorinated water stand open to the air for 24 hours before using.

1: Appl Environ Microbiol. 1979 Nov;38(5):840-5.

Influence of fulvic acid on bacteriophage adsorption and complexation in soil.

- **Bixby RL**,
- **O'Brien DJ**.

The effect of fulvic acid, the major fraction of natural soluble organic matter, on the adsorption of MS2 bacteriophage to soil was investigated in controlled laboratory experiments. **Batch experiments together with scanning electron microscopy-**

energy-dispersive X-ray analysis showed that fulvic acid complexed phage, which prevented its adsorption to soil. Phage strongly adsorbed to soil in the absence of fulvic acid. Phage which was complexed with fulvic acid was not irreversibly inactivated and could become viable under proper conditions, illustrating the importance of assay and elution procedures in the recovery of virus from aqueous solutions.

This is an older study. I would think that the influence of FA on preventing viral adhesion to cells would be next, but I would not be surprised if subsequent research has remained proprietary to the companies conducting it.

PMID: 396884 [PubMed - indexed for MEDLINE]

: J Mol Evol. 1975 Dec 29;6(4):253-70.

On the possible role of organic melanoidin polymers as matrices for prebiotic activity.

- **Nissenbaum A**,
- **Kenyon DH**,
- **Oro J**.

One of the major diagenetic pathways of organic matter in recent sediments involves the condensation of cellular constituents, particularly amino acids and sugars, into insoluble melanoidin-type polymers. These polymers consist mainly of humic and fulvic acids and make up the major part of the organic carbon reservoir in recent sediments. We suggest that a similar set of reactions between abiotically formed amino acids and sugars, and more generally between aldehydes and amines, occurred on a large scale in the **prebiotic hydrosphere**. The rapid formation of this insoluble polymeric material would have removed the bulk of the dissolved organic carbon from the primitive oceans and would thus have prevented the formation of an "organic soup". **Melanoidin polymers have several properties which make them attractive hypothetical precursors of contemporary oxidation-reduction coenzymes: 1. they contain heterocyclic nitrogen compounds similar to the nitrogenous bases; 2. they contain a high concentration of stable free radicals; and 3. they tend to concentrate those heavy metals which play prominent roles in contemporary enzymic redox processes. The prebiotic formation of similar polymers could, therefore, have provided the starting point for a basic class of biochemical reactions.** We suggest that the prebiotic scenario involved chemical and protoenzymic reactions at the sediment-ocean interface in relatively shallow waters and under conditions not much different from those of the recent environment.

PMID: 1542 [PubMed - indexed for MEDLINE]

Fascinating – humic substances as precursor molecules in replicative biosynthesis. However, humic substances have been found to be the result of extensive microbial degradation in much research prior to and after this 1975 study. In other words FA is a post-biotic, not a prebiotic.

But billions of years ago the "prebiotic" world was a much different environment – a reducing atmosphere and the lack of established enzymatic pathways limited molecular synthesis to slow anaerobic chemical pathways. Perhaps in that "reverse environment" (chemical-anaerobic vs biological-aerobic) a slow synthesis of humic-like carbonaceous substances did occur.

If so humic substances could provide varying functional group environments for the binding and release of subtrates and cofactors (adjacent metal complexes), and thereby "catalyze" the synthesis of complex proteins.
We use light humics today to complex and deliver nutrient metals to plants and animals.