

Effects of Fulvic Acid on Skin

A brief literature review – Michael Karr, Ph.d

Why Use Fulvic Acid in Skin Care Products?

Fulvic acid has been demonstrated to be useful for a wide variety of skin related conditions:

- psoriasis, eczema, seborrheic keratosis, pruritis and actinic keratosis
- Has anti-bacterial, anti-fungal, and anti-viral properties
- Has anti-inflammatory and anti-allergic properties
- Stimulates healing
- Useful in treatment of allergic diseases
- Anti-mutagenic and anti-clastogenic effects, preventing genetic material from mutating - a key factor in skin cancer prevention

Topics:

- *Various Skin Conditions Effectively Treated by Humic Substances*
- *Antibacterial Activity*
- *Antiviral Activity*
- *Antifungal Activity*
- *Anti-Inflammatory Properties of Fulvic Acid*
- *Allergies and Allergic Reactions*
- *Antimutagenic – Desmutagenic Anticlastogenic and Antitoxic effects*
- *Fulvic Acids as a Skin Penetrant*
- *Skin Toxicity and Irritation Levels of Humic Substances*
- *Comparison of CellxCell Fulvic to Another Fulvic Source Material Used in Skin Therapy*

Brief Notes: The literature presented below is meant to be a summary of the research findings, including patents. For more information on the specifics of any paper, the full reference precedes the cited segments.

It is also assumed that the user of this document will respect the intellectual property rights of any information revealed from patents and copyrighted material.

Various Skin Conditions Effectively Treated by Humic Substances

Compositions and methods of treatment using peat derivatives

United States Patent 6,267,962

Inventor: Hart , et al.

Publication date: July 31, 2001

“The term peat, as used herein, refers generally to microbial degradation products of plants, including peat and peat-derived materials, coal, and coal-derived materials. These materials include humic acids and **fulvic acids**, which are isolated from peat. Coal-derived material includes leonardite and lignite. *In* “BACKGROUND OF THE INVENTION”

The active compositions according to the present invention, are referred to herein as **PAFs (Peat Active Factors)**. **PAFs are isolated by extraction of peat fractions...***(Here they use the standard base-acid extraction methods.)* *In* SUMMARY OF THE INVENTION

PAFs have been demonstrated to be useful for the treatment of a wide variety of diseases and disorders. **In particular, PAFs have been found to be active for the treatment of psoriasis, eczema, seborrheic keratosis, pruritis and actinic keratosis and; as an anti-inflammatory; topical analgesic; and stimulator of wound healing. In addition, it has antibacterial, antifungal, and antiviral properties and is useful in the prevention and treatment of acne, cold sores, conjunctivitis, and athlete's foot.**

Veterinary uses of PAFs include use as an anti-inflammatory and analgesic and as an aid to healing of dermatitis and open wounds. In addition, PAFs are useful in treating inflammation caused by flea bites. *In* DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

PAFs have been found to be particularly effective in ameliorating the itching and plaques of psoriasis and eczema and the pain of burns and other skin wounds in humans. Although not intended to be limiting, it is hypothesized that the PAFs are active against skin diseases and other skin disorders due to their ability to inhibit or modulate the activity of PKC and related components or targets of the arachidonic acid cascade. *In* DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

The following study is reviewed under the “Anti-Inflammatory Properties of Fulvic Acid” section, but also contains the results of studies on specific skin conditions:

Fulvic acid and its use in the treatment of various conditions

United States Patent 6,569,900

Inventor: Dekker , et al.

Publication date: May 27, 2003

Antibacterial Activity

Bacteriostatic and bactericidal composition

European Patent Publication number: GB2244215

Publication date: 1991-11-27

Inventor: CRONJE et. al.

Abstract:

A composition which has bactericidal or bacteriostatic properties comprises coal-derived fulvic acid or a salt or a derivative thereof as active ingredient in a suitable carrier. The carrier is preferably water.

Bacteriostatic and bacteriocidal method using fulvic acid derivatives

United States Patent 5,204,368

Inventors: Cronje, et al.

Patent Issued: April 20, 1993

Abstract:

The present invention relates to compounds of the class of **coal-derived fulvic acid** or a salt or a derivative thereof as active ingredient in a suitable carrier, **useful as a bactericidal or bacteriostatic agent**. The carrier is preferably water.

The use of bactericides is one of the most effective ways to prevent biofouling and the concomitant corrosion. In a field trial, it was found that **oxifulvic acid I was more effective in controlling the growth and proliferation of microorganisms in industrial water cooling systems than Bio Met**. In: METHODOLOGY FOR EVALUATION OF BIOCIDAL ACTIVITY

Anesio, AM and Hollas, C and Graneli, W and J. Laybourn-Parry. 2004. **Influence of humic substances on bacterial and viral dynamics in freshwaters** Applied and Environmental Microbiology, Volume: 70, Number: 8, Pages: 4848-4854

Abstract:

Bacterial and viral abundances were measured in 24 lakes with dissolved organic carbon (DOC) concentrations ranging from 3 to 19 mg of C liter(-1). In addition, a laboratory experiment was performed to test the effects of different sources of carbon (i.e., glucose and fulvic acids) and nutrients on the dynamics of viruses and bacteria. In the lake survey, no correlation was found between virus abundance and DOC concentration, yet there was a significant positive correlation between bacterial abundance and DOC concentration. A negative correlation was found between the virus-to-bacteria ratio and DOC level. **These results are in agreement with our findings in the laboratory, where virus counts were significantly lower in treatments with fulvic acid additions than in a control (mean, 67.4% +/- 6.5% of the control)**. Virus counts did not differ significantly among the control and treatments with glucose, indicating that it was the type of organic carbon and not quantity which had an impact on viruses. Results from this study suggest that the way viruses control bacterial assemblages in humic lakes is different from the mechanism in clear water systems.

Antiviral Activity

Fulvic acid and its use in the treatment of viral infections

European Patent Publication number: EP1698333

Publication date: 2006-09-06

Inventor: DEKKER JOHANNES (ZA); MEDLEN CONSTANCE ELIZABETH (ZA)

Abstract:

A pharmaceutical composition comprising fulvic acid, salt, ester or derivative thereof as active agent is disclosed. The composition is preferably administered orally or topically for treating a condition in a human or animal. The condition may, for example, be inflammation, acne, eczema or bacterial or fungal or viral infections.

Antifungal Activity

Fujita K, Nagamine Y, Ping X, and M. Taniguchi M. 1999. **Mode of action of anhydrofulvic acid against *Candida utilis* ATCC 42402 under acidic conditions.** J Antibiot (Tokyo). 1999 Jul;52(7):628-34

Abstract:

The mode of action of anhydrofulvic acid against *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.**

The following patent refers to the treatment of *Candida*, which is the name for a group of yeasts (a type of fungus) that commonly infect the skin. Candidal skin infections include:

- Oral candidiasis (oral thrush)
- Vulvovaginal candidiasis (genital infection in women) including cyclic vulvovaginitis
- Balanitis (penile infection)
- Intertrigo (skin fold infections)
- Napkin dermatitis (nappy or diaper rash)
- Chronic paronychia (nail fold infection)
- Onychomycosis (nail plate infection)
- Chronic mucocutaneous candidiasis

Fulvic acid and its use in the treatment of candida infections

Publication number: EP1700599

Publication date: 2006-09-13

Inventor: DEKKER JOHANNES (ZA); MEDLEN CONSTANCE ELIZABETH (ZA)

Abstract:

A pharmaceutical composition comprising fulvic acid, salt, ester or derivative thereof as active agent is disclosed. The composition is preferably administered orally or topically for treating a condition in a human or animal. The condition may, for example, be inflammation, acne, eczema or bacterial or fungal or viral infections.

Claims

1. The use of fulvic acid, salt, ester or derivative thereof in the manufacture of a medicament for treatment in humans and animals of candida infections.
 2. The use according to claim 1 wherein the candida infection is *Candida albicans*.
 3. The use according to either of claims 1 or 2 wherein the medicament is for oral or topical administration.
 4. The use according to claim 3 wherein the medicament is provided in the form of a solution, paste, ointment, powder or any other form suitable for topical administration.....
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Anti-Inflammatory Properties of Fulvic Acid

Fulvic acid and its use in the treatment of inflammation

European Publication number: EP1700600

Publication date: 2006-09-13

Inventor: DEKKER JOHANNES (ZA); MEDLEN CONSTANCE ELIZABETH (ZA)

Abstract:

A pharmaceutical composition comprising fulvic acid, salt, ester or derivative thereof as active agent is disclosed. The composition is preferably administered orally or topically for treating a condition in a human or animal. The condition may, for example, be inflammation, acne, eczema or bacterial or fungal or viral infections.

My Note: For this patent, I have decided to include some of the specific trial results, because they are a good example of the types that exist in many of the other references cited in this short review. Note also the antimicrobial properties and skin conditions treated in the trials.

Fulvic acid and its use in the treatment of various conditions

United States Patent 6,569,900

Inventor: Dekker, et al.

Publication date: May 27, 2003

Abstract:

Fulvic acid salts, esters or derivatives thereof in pharmaceutical preparations are effective for treating inflammation, acne, exzema or bacterial or fungal or viral infections. These pharmaceutical preparations may be given either orally or topically in the form of a solution, paste, ointment, powder to humans or animals.

“The fulvic acid is preferably a **fulvic acid derived from a hot wet coal oxidation process** of the type described in U.S. Pat. No. 4,912,256. Such a fulvic acid is hereinafter referred to as "**oxifulvic acid** or OFA".

Evaluation of Oxifulvic Acid as an Anti-Inflammatory Compound In Vivo

1. Evaluation in Dinitrofluorobenzene Sensitized Mice

No signs of toxicity was observed during the two days of treatment with the two oxifulvic acid creams.

2. Evaluation in Pyotraumatic Dermatitis in Cats and Dogs

Ten clinical cases were entered in the trial. **To qualify for this trial the following entities had to be present on the skin of the animals: wheal, erythema, pruritis and pyogenesis.** Lesions were classified as slight, mild or severe before treatment. No other treatment was allowed during the trial. Owners were supplied with the **9% oxifulvic acid cream** and instructed to **apply the cream twice a day** to the affected areas. This treatment had to **continue for seven days**. The owners were asked to return exactly seven days after the treatment commenced and the cases were reevaluated clinically, biopsied and photographed.

Decreased inflammation was observed clinically as well as pathologically in all 10 cases studied as can be seen from the histopathological investigation described hereinafter. No side effects were noted in any of the cases. In most cases it was noted that resolutions of the lesions were complete and did not recur. Only in one of the cases, described as a chronic and longstanding case, did the owner return after 3 days because the dog was still scratching extensively. In addition, the biopsy lesions of the first biopsy were completely healed.

Another 2 trial descriptions:

The **antimicrobial** properties of an oxifulvic acid solution (25.4 percent by mass of the fulvic acid) and a 4.5 percent by mass oxifulvic acid cream were evaluated in vitro on a number of well known pathogens.

Further, the efficacy of the 4.5 percent oxifulvic acid cream and a 25.4 percent by mass oxifulvic acid solution **to inhibit the growth of bacteria and fungi** was tested in accordance with the SABS method 730 (in vitro) on a few test organisms.

Their quote: “From the foregoing studies it can be seen that oxifulvic acid exhibits some measure of **antimicrobial activity or bacteriostatic or fungistatic efficacy against some of the test organisms, even when formulated in a cream.**”

Constance E.J. Van Rensburg, Susan C.K. Malfeld, and Johan Dekker. **2001. Topical application of oxifulvic acid suppresses the cutaneous inflammatory response in mice.** Drug Development Research v. 53, #1, Pages 29 – 32. 2001. Published Online: 26 Jul 2001.

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 diclofenac 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.

Allergies and Allergic Reactions

Yamada P, Isoda H, Han JK, Talorete TP, Yamaguchi T, and Y. Abe . **Inhibitory Effect of Fulvic Acid Extracted from Canadian Sphagnum Peat on Chemical Mediator Release by RBL-2H3 and KU812 Cells.** Biosci Biotechnol Biochem. 2007 May 7;

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-dimethylthiazol-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.**

Antimutagenic – Desmutagenic Anticlastogenic and Antitoxic effects

G. Ferrara, E. Loffredo, N. Senesi and R. Marcos: 2006.

Humic acids reduce the genotoxicity of mitomycin C in the human lymphoblastoid cell line TK6 . *Mutat Res.* 2006 Jan 31;603(1):27-32. Epub 2005 Dec 28.

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 µg/ml, in three different treatments: (1) HA alone (genotoxic test); (2) HA after 2-h pre-incubation with 0.3 µM of MMC (desmutagenic test) and (3) combinations of HA and MMC at 0.3 µM 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 cytotoxicity 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.**

Ferrara, G., Loffredo, E. and N. Senesi 2004. **Anticlastogenic, antitoxic and sorption effects of humic substances on the mutagen maleic hydrazide tested in leguminous plants.** European J. of Soil Science, v. 55, # 3, September 2004, pp. 449-458(10)

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 anelophases (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.****

Fulvic Acids as a Skin Penetrant

Beer AM, Junginger HE, Lukanov J, and P. Sagorchev 2003. **Evaluation of the permeation of peat substances through human skin in vitro.** Int J Pharm. 2003 Mar 6;253(1-2):169-75.

Abstract:

Peat and various peat extracts have been successfully applied for a variety of clinical indications..... The effects are, however, dependent on the possible permeability of pharmacologically active substances as naturally occurring ingredients of peat.....

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 on smooth muscle is dependent on the permeated fraction. Especially, the HPLC fractions 7-11 and 14 are able to permeate human skin....**Fraction 14 (the lightest) shows the strongest stimulatory effect**

These results show that the cutaneous therapy with peat treatment results in transcutaneous permeation of biologically active fulvic and ulmic acid derivatives explaining the additional "chemical" effect of peat treatment in clinical practice.

Skin Toxicity and Irritation Levels of Humic Substances

Czyzewska-Szafran H, Jastrzebski Z, Sołtysiak-Pawluczuk D, Wutkiewicz M, Jedrych A, and M. Remiszewska 1993. **Systemic toxicity and dermal irritation of Tolpa Peat Preparation.** Acta Pol Pharm. 1993;50(4-5):373-7.

Abstract:

The systemic toxicity of the peat preparation in rats and rabbits was assessed. **Dermal irritation tests were conducted on rabbits. In acute and chronic toxicity studies Tolpa Peat Preparation was well tolerated in both animal species.** Laboratory findings revealed no hematologic abnormalities as well as disturbances in liver and kidney function. No local irritancy of TPP was found. **The results show that TPP may be considered as practically non toxic.**

Wiegleb K, Lange N, and M Kühnert. 1993. **The use of the HET-CAM test for the determination of the irritating effects of humic acids.** Dtsch Tierarztl Wochenschr. 1993 Oct;100(10):412-6. [German]

Abstract:

Using the synthetic humic acid product HS 1500 and the native product Sodium-Humate, the suitability of the HET-CAM-test to evaluate irritating effects was tested. **Neither sensitizing nor irritating properties were detectable in concentrations of up to 10% in either humic acid solution.** This leads us to the conclusion that both products are very mildly acting substances on mucous membranes and skin, causing no irritative effects.

Comparison of CellxCell Fulvic to Another Fulvic Source Material Used in Skin Therapy

United States Patent 6,440,436 Ghosal August 27, 2002 **Process for preparing purified shilajit composition from native shilajit**

Abstract

A purified shilajit composition is provided herein from native shilajit. The composition has an abundance of bioactive components, particularly, at least 0.3%, preferably 0.4-1%, by weight, oxygenated dibenzo- α -pyrones and at least 60%, preferably 65-70%, by weight of fulvic acids of **low-to-medium molecular weight (Mn of 700-2000) with an E4 /E6 ratio of 8-10 at 465-665 nm**, and whose 2% aqueous solution has a pH of ≈ 7 . Personal care, pharmaceutical and nutritional use formulations of the purified shilajit composition also are described.

My Note: Our fulvic acids have similar molecular weights, but a much higher E4 /E6 ratio of 17 - 20 at 465-665 nm, which represent lighter fulvic acid molecules of material. Furthermore, our process does not use harsh chemicals for extraction, and has the technological advantages for us to be able to produce high volumes at low costs.

I have not yet found the E4/E6 ratios of peat extracts, or PAFs in the literature. However the International Humic Substances Society (IHSS) does have a fulvic acid extract from peat with an E4/E6 ratio of 14.