

# Clinical abstracts

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## Pharmacologically active ingredients

### **Isozymes Of Superoxide Dismutase From Aloe Vera**

**Sabeh F; Wright T; Norton SJ**

Department Of Biological Sciences, University Of North Texas

*Enzyme Protein 49(4):212-21 1996*

**E**xtracts from the parenchymatous leaf gel and the rind of the Aloe vera plant (*Aloe barbadensis* Miller) were shown to contain seven electrophoretically-identifiable superoxide dismutases (SODs). The chromatographic elution profiles and the migration of these bands on native polyacrylamide gel electrophoresis (PAGE), for both the gel and rind, are quite similar. Two of these seven activities are insensitive to cyanide treatment, suggesting that they are manganese-SODs. The other five activities are sensitive to cyanide treatment, but insensitive to azide treatment and are presumed to be cupro-zinc SODs. All of the seven proteins appear to be homodimers with apparent native molecular masses centered at approximately 32 and 42 kD as indicated by SDS-PAGE and gel-filtration (FPLC) chromatography. The specific activities of SODs in the *A. vera* rind and gel are comparable to those of spinach leaves and of rabbit liver.

### **Aspergillus Nidulans verA Is Required For Production Of The Mycotoxin Sterigmatocystin**

**Keller NP; Kantz NJ; Adams TH**

Department Of Plant Pathology & Microbiology, Texas A&M University

*Appl Environ Microbiol Vol 60, ISS 5, 1994, P1444-50*

**A***sp*erillus *nidulans* produces the carcinogenic mycotoxin sterigmatocystin (ST), the next-to-last precursor in the aflatoxin (AF) biosynthetic pathway found in the closely related fungi *Aspergillus flavus* and *Aspergillus parasiticus*. We identified and characterized an *A. nidulans* gene, *verA*, that is required for converting the AF precursor versicolorin A to ST. *verA* is closely related to several polyketide biosynthetic genes involved in polyketide production in *Streptomyces* spp. and exhibits extended sequence similarity to *A. parasiticus ver-1*, a gene proposed to encode an enzyme involved in converting versicolorin A to ST. By performing a sequence analysis of the region 3' to *verA*, we identified two additional open reading frames, designated ORF1 and ORF2. ORF2 is closely related to a number of cytochrome P-450 monooxygenases, while ORF1 shares identity with the gamma subunit of translation elongation factor 1. Given that several steps in the ST-AF pathway may require

monooxygenase activity and that AF biosynthetic genes are clustered in *A. flavus* and *A. parasiticus*, we suggest that *verA* may be part of a cluster of genes required for ST biosynthesis. We disrupted the *verA* coding region by inserting the *A. nidulans argB* gene into the center of the coding region and transformed an *A. nidulans argB2* mutant to arginine prototrophy. Seven transformants that produced DNA patterns indicative of a *verA* disruption event were grown under ST-inducing conditions, and all of the transformants produced versicolorin A but negligible amounts of ST (200-fold to almost 1,000-fold less than the wild type), confirming the hypothesis that *verA* encodes an enzyme necessary for converting versicolorin A to ST.

## **Purification & Characterization Of A Glutathione Peroxidase From The Aloe Vera Plant**

**Sabeh F; Wright T; Norton SJ**

Dep. Biol. Sci., Univ. North Texas

*Enzyme Protein (1994) Volume Date 1993, 47 (2), 92-8*

**E**xts. from the parenchymous leaf-gel of the Aloe vera plant (*Aloe barbadensis* Miller) were shown to contain glutathione peroxidase (GSHPx) activity. The activity was purified to homogeneity by ion exchange and gel filtration (FPLC) chromatog. in the presence of 0.5 mM glutathione. The native enzyme has an apparent mol. wt. of 62 kD as detd. by gel filtration. In the presence of SDS, the mol. wt. was estd. to be about 16 kD as detd. by SDS-PAGE. The native enzyme is proposed to be constituted of four identical subunits; it also contains one atom of selenium per subunit, as found with most glutathione peroxidases from animal sources. The Km values were detd. to be 3.2 mM for glutathione and 0.26 mM for the hydroperoxide substrate, cumene hydroperoxide. The enzyme is competitively inhibited by N, S-bis-FMOC glutathione ( $K_i = 0.32$  mM), a potent inhibitor of glyoxalase II. Inhibitors of glyoxalase I (e.g., S-octylglutathione) have no effect on the peroxidase activity.

## **Chemical Studies Of Aloe Vera Juice**

**Gjerstad, Gunnar; Bouchey GD**

*Quarterly Journal of Curde Drug Research 1968 Vol 964. p. 1451*

**I**n 1968, Gjerstad and Bouchey conducted a series of studies to determine the mineral constituents of Aloe vera and found the principal inorganic elements in the juice were calcium, chlorine, sodium, potassium, and manganese.

Then in 1971, the same two researchers conducted a study of amino acids present in Aloe vera juice, coming to the conclusion that it contained the mucopolysaccharides, glucose, and aldontose, along with 18 of the 22 amino acids known to be necessary in the human body. They concluded further that one tablespoon of Aloe vera gel would contain in excess of 75 different chemical ingredients, although they identified few outside their occurrence in specified groupings.

## **The Glucomannan System From Aloe Vahombe (Liliaceae) III. Comparative Studies On The Glucomannan Components Isolated From The Leaves**

**Vilkas E; Radjabi-Nassab F**

*Biochimie 68(9):1123-7 1986 Sep*

The polysaccharide mixture obtained by hot water extraction of Aloe vahombe leaves is composed of at least four different partially acetylated glucomannans which differ in molecular weight, glucose to mannose ratios and acetyl contents. Furthermore, one fraction contains a small but significant amount of protein which could not be removed by gel filtration in a hydrogen-bond-breaking medium, by DEAE-Sephadex A-50 anion exchange chromatography, or by Sevag's method.

## **Orientation Of Interphase Chromosomes As Detected By Giemsa C-Bands**

**Ghosh S; Roy SC**

*Chromosoma 61(1):49-55 1977 Apr 27*

The orientation of Giemsa C-bands has been studied in mitotic and interphase cells of *Allium cepa*, *A. sativum* and of *Aloe vera*. The C-bands in these three species are located at the telomeres, secondary constriction region of the nucleolar chromosomes and the centromeric regions, respectively. Observations in *A. cepa* and *Aloe* indicate clearly that the interphase chromosomes are non-random in their orientation and possibly maintain their telophase configuration through the attachment of telomeres and perhaps of kinetochores with the nuclear membrane. Electron micrographs of onion cells also reveal that certain heterochromatic segments are associated with the nuclear membrane. The nucleolar interstitial C-bands in *A. sativum* remain free in the nucleoplasm and may come close to each other due to heterochromatic attraction. Such a heterochromatic attraction is also evident between telomeric regions and between centromeres. However, a two by two attachment could not be noticed. A diagrammatic representation of the orientation of interphase chromosomes has been presented.

## **Purification Of Active Substances Of Aloe Arborescens Miller & Their Biological & Pharmacological Activity**

**Saito, Hiroko**

Dep. Pharm., Aichi Cancer Center

*Phytother Res. (1993) 7 (Spec. Issue, Proceedings of the International Congress of Phytotherapy, 1991), S14-S19*

The authors purified Aloctin A from *Aloe arborescens* Miller and defined its chem., biol. and pharmacol. activities. Aloctin A consists of two discrete bands, a and b with a combined S-S bond. Its mol. wt. for a is 7500 and the mol. wt. for b is 10,500. Aloctin A has many biol. and pharmacol. activities as follows: 1. hemagglutinating activity; 2. cytoagglutinating activity; 3. mitogenic activity of lymphocytes; 4. ppt. - forming reactivity with  $\alpha_2$ -macroglobulin; 5. complement C3 activating activity; 6. inhibition of heat-induced hemolysis of rat erythrocytes; 7. anti-tumor effect; 8. anti-inflammatory effect; 9. inhibition of gastric secretion and gastric lesions.

## **The Molecular Structure Of Iso-Aloesin Isolated From The Leaves Of Aloe Vera L. Var. Chinensis (Haw.) Berge**

**Yuan AX**

Guanxi Institute Of Traditional Chinese Medical & Pharmaceutical Sciences

*Chung Kuo Chung Yao Tsa Chih (1993 Oct) 18 (10) 609-11, 639*

A new constituent iso-aloesin was isolated from the leaves of Aloe vera var. chinensis found in the Province of Guangxi. The molecular formula of iso-aloesin is C<sub>19</sub>H<sub>22</sub>O<sub>9</sub>, which is 2-acetyl-6-C-beta-D-glucopyranosyl-7-hydroxy-5-methyl-chromone.

## **A Phytochemical Study Of Aloe Vera Leaf**

**Rowe, Tom D; Parks, Lloyd M**

*Journal of the American pharmaceutical Association 1939 Vol 21 pp. 538-539*

In 1939, professor Tom D. Row, Lloyd M. Parks, and associates made a breakdown of Aloe vera which would prove to be the most extensive to that time. Believing that the real curative properties would be found in the rind rather than the gel, Rowe and Parks isolated the following components: the hydrolyzing enzymes oxydase, catalase, and amylase; beta carotene (a pro-vitamin of vitamin A); the starch-splitting enzyme, pentosan; calcium oxalate; a mineral based cleansing agent. They also isolated many of the anthraquinones discovered earlier by Chopia and Gosh as well as traces of other vitamins and minerals.

## **Biological Activity Of Aloe Vera**

**Davis, Robert H**

Dep. Biomed. Sci., Pennsylvania Coll. Podiatr. Med.

*Seifen, Oele, Fette, Wachse (1993) 119(11), 646, 648-9*

Some of the constituents of Aloe vera (AV) have biol. activity similar to amino acids, vitamin C and growth factors like gibberellin and auxin. The AV mol. probably does not act alone, but rather acts in either an additive or synergistic fashion with some of the 100 constituents of the AV.

## **Glyoxalase I & Glyoxalase II From Aloe Vera: Purification, Characterization & Comparison With Animal Glyoxalases**

**Norton SJ; Talesa V; Yuan WJ; Principato GB**

Department Of Biochemistry, University Of North Texas

*Biochem Int 22(3):411-8 1990 Nov*

Glyoxalase I and glyoxalase II from the outer green rind of Aloe vera leaves were purified by (matrix) affinity ligand-enzyme binding methods. The purified enzymes exhibited single

protein bands on SDS-PAGE electrophoresis, with MW values of approximately 44,000 and 27,000 for glyoxalase I and glyoxalase II, respectively. The glyoxalase I is a basic protein (pI 7.8), while the glyoxalase II (3 protein bands) is acidic (pI 4.7, 4.8 [prevalent form], and 5.0). The kinetic constants,  $K_m$  and  $V_{max}$ , and  $K_i$  values for certain inhibitors are reported for both glyoxalase I and glyoxalase II. The glyoxalase enzymes from Aloe vera were compared with reported animal and plant glyoxalases.

### **Antibradykinin Active Material In Aloe Saponaria**

**Yagi A; Harada N; Yamada H; Iwadare S; Nishioka I**

*J Pharm Sci 71(10):1172-4 1982 Oct*

A material having antibradykinin activity on isolated guinea pig ileum was partially purified from the nondialysate of the pulp of Aloe saponaria by repetition of gel chromatography using a hydrophilic polyvinyl gel and dextran gels. From the results of amino acid and carbohydrate analyses, the antibradykinin-active material was estimated to be a glycoprotein. It was found that this material catalyzes the hydrolysis of bradykinin at pH 7.4. The results of peptide analysis using reversed-phase high-performance liquid chromatography coupled with amino acid analysis indicate that this glycoprotein cleaves the Gly4-Phe5 and Pro7-Phe8 bonds of the bradykinin molecule.

### **Effect Of Aloe Lectin On Deoxyribonucleic Acid Synthesis In Baby Hamster Kidney Cells**

**Yagi A; Machii K; Nishimura H; Shida T; Nishioka I**

*Experientia 41(5):669-71 1985 May 15*

A homogeneous glycoprotein (mol. wt 40,000) containing 34% carbohydrate was isolated from Aloe arborescens var. natalensis. At a concentration of 5 micrograms/ml, this glycoprotein was shown to stimulate deoxyribonucleic acid (DNA) synthesis in baby hamster kidney (BHK) cells and to have the properties of a lectin which reacts with sheep blood cells. The chemical and physical properties of the glycoprotein (Aloe lectin) are also discussed.

### **Isolation Of S cDNA For A Phosphoenolpyruvate Carboxylase From A Monocot CAM-Plant, Aloe Arborescens: Structure & Its Gene Expression**

**Honda H; Okamoto T; Shimada H**

Life Science Institute, Mitsui Toatsu Chemicals, Inc.

*Plant Cell Physiol 37(6):881-8 1996 Sep*

A phosphoenolpyruvate carboxylase (PEPCase) cDNA was isolated from Aloe arborescens, a monocot CAM plant. Northern analysis of the PEPCase transcript indicated that it is specifically expressed in green leaves, strongly suggesting its involvement in CAM photosynthesis. No diurnal change in expression level was evident. Western blot analysis also showed no alteration of the amount of the PEPCase protein. These results suggest that circadian rhythm in PEPCase activity may be regulated post-translationally. The representative cDNA clone contained an ORF encoding 964 amino acid residues. Deduced

amino acid sequence of the Aloe PEPCase is highly conserved as compared with other PEPCases. The phosphorylation site which may be modified by PEPC-kinase was conserved. An evolutionary map with known PEPCases suggested that CAM-type PEPCases were located between C4 and housekeeping PEPCases.

### **Further Studies Of The Glucomannan From Aloe Vahombe (Liliaceae) II. Partial Hydrolyses & NMR 13C Studies**

**Radjab-Nassab F; Ramiliarison C; Monneret C; Vilkas E**

*Biochimie 66(7-8):563-7 1984 Jul-Aug*

The polysaccharide from Aloe vahombe (lilaceae) was submitted to partial hydrolyses by sulfuric, oxalic and phosphoric acid. Some oligosaccharides were isolated and investigated by chemical and 13C NMR spectroscopic methods. Their structure was determined. The results prove unambiguously that in some oligosaccharides were isolated and investigated by chemical and 13C NMR spectroscopic methods. Their structure was determined. The results prove unambiguously that in the analyzed material the D-mannose is linked to the D-glucose by beta-1—4 linkages to form a carbohydrate heteropolymer.

### **Bioactive Anthraquinone Glycosides From Picramnia Antidesma Spp. Fessonia**

**Solis PN; Ravelo AG; Gonzalez AG; Gupta MP; Phillipson JD**

Department Of Pharamacognosy, School Of Pharmacy

*Phytochemistry 38(2):477-80 1995 Jan*

A bioactivity guided fractionation, using KB cells and brine shrimp assays, of the methanolic extract from the leaves of Picramnia antidesma yielded two known anthraquinones, Aloe-emodin and Aloe-emodin anthrone, and three new Aloe-emodin C-glycosides, named picramnioside A, picramnioside B and picramnioside C. Structures were established by spectroscopic methods (UV, IR, mass spectrometry, 1H and 13C and 2D NMR including COSY 45, HMQC, HMBC and ROESY). CD was used to establish the absolute configuration of the picramniosides.

### **Pharmacokinetic-Metabolic Studies With 14C-Aloe Emodin After Oral Administration To Male & Female Rats**

**Lang W**

Department Of Radiobiochemistry, Madaus AG

*Pharmacology 47 Suppl 1():110-9 1993 Oct*

After oral administration of 4.5 mg/kg 14C-Aloe emodin (AE) to rats 20-30% of the dose was excreted in urine and the rest in feces. AE was quickly metabolized to rhein, to an unknown metabolite and to conjugates of all three. In the plasma about 10% of 14C-activity was identified as free AE. Maximum plasma values were reached 1.5-3 h p.a. with 248 (male) and 441 (female) ng equivalents AE/ml. Maximum concentrations in plasma were about 3

times higher than those in ovaries and 10 times higher than those in testes. Only liver, kidney and intestinal tract showed higher concentrations than plasma. Terminal half-life (for radioactivity) in blood was about 50 h.

### **Genotoxicity Of Naturally Occurring Hydroxyanthraquinones**

**Westendorf J; Marquardt H; Poginsky B; Dominiak M; Schmidt J; Marquardt H**

Department Of Toxicology, University Of Hamburg Medical School

*Mutat Res Vol 240, ISS 1, 1990, P1-12*

A variety of structurally related hydroxyanthraquinones (HA) were investigated in a test battery for the evaluation of mutagenicity and cell-transforming activity. The tests were: (1) the Salmonella typhimurium mutagenicity assay, (2) the V79-HGPRT mutagenicity assay, (3) the DNA-repair induction assay in primary rat hepatocytes and (4) the in vitro transformation of C3H/M2 mouse fibroblasts. In Salmonella, most of the tested compounds were mutagenic in strain TA1537, but only a few were active in other strains. Among these were HA with a hydroxymethyl group, such as lucidin and Aloe-emodin. In V79 cells, only HA with 2 hydroxy groups in the 1,3 positions (1,3-DHA, purpurin, emodin) or with a hydroxymethyl sidechain (lucidin and Aloe-emodin) were mutagenic. The compounds found to be active in V79 cells were also active in the DNA-repair assay and in the C3H/M2 transformation assay. Thus, it appears that the genotoxicity of HA is dependent on certain structural requirements.

### **Mechanochemical Solid State Reactions Of Natural Products For Medicinal Use Containing Hydroxyanthraquinone Derivatives**

**Kuzuya M; Sakata H; Kondo S; Noguchi A**

Gifu Pharmaceutical University

*Yakugaku Zasshi 111(11):665-71 1991 Nov*

In commercial powdered natural products for medicinal use containing various combined forms of hydroxyanthraquinone derivatives such as Sennae Folium, Cassiae Semen, Rhei Rhizoma and Aloe a considerable amount of stable free radicals (ca.  $10^{17}$ - $10^{18}$  spin/g) was found to be contained by use of electron spin resonance (ESR) spectral measurements. It was also found that the vibratory milling of such powders in a metallic vessel enhanced the ESR spectral intensities, demonstrating the occurrence of mechanoradical formation. Separate experiments also demonstrated that the vibratory milling of various kinds of powdered hydroxyanthraquinone derivatives mixed with calcium oxalate has produced the mechanoradicals effectively, but they decayed gradually on standing at room temperature. It was suggested, therefore, that the mechanoradicals formed in the above natural products are metal complexes of the corresponding semiquinone anion radicals induced by solid state one electron transfer mechanism from the active metal surface, part of which is further immobilized in polymeric fibers or the like in the plant tissues.

## **Aloe Vera**

**Klein AD; Penneys NS**

Department Of Dermatology, University Of Miami School Of Medicine

*J Am Acad Dermatol, 18(4 Pt 1):714-20 1988 Apr*

**W**e reviewed the scientific literature regarding the Aloe vera plant and its products. Aloe vera is known to contain several pharmacologically active ingredients, including a carboxypeptidase that inactivates bradykinin in vitro, salicylates, and a substance(s) that inhibits thromboxane formation in vivo. Scientific studies exist that support an antibacterial and antifungal effect for substance(s) in Aloe vera. Studies and case reports provide support for the use of Aloe vera in the treatment of radiation ulcers and stasis ulcers in man and burn and frostbite injuries in animals. The evidence for a potential beneficial effect associated with the use of Aloe vera is sufficient to warrant the design and implementation of well-controlled clinical trials.

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