

XVI

REPRINTED FROM:



PROCEEDINGS OF THE

# INTERNATIONAL CANCER CONGRESS

New Delhi (India), October 30 - November 5, 1994

Editors

R.S. RAO, M.G. DEO and L.D. SANGHVI  
I. MITTRA (Co-ordinator)



MONDUZZI EDITORE

INTERNATIONAL PROCEEDINGS DIVISION

# Preliminary results for some responses in cancers with metal-carbonyl compounds under associated immunotherapy. Metal-FLNT4 complex (Zn, Fe, V. others)

XVI International  
Cancer Congress  
1994

New Delhi, India  
30 Oct. - 5 Nov. 1994

M. GRANDI, C. ASSOUN \*, R.A. CANUTO \*\*,  
P. COURRIERE \*\*, P. SOULA \*\*,  
M. MAGGIORA \*\* and A. LACIVITA

*La Torre Centro Studi Ricerche e Terapia delle Neoplasie, Torino (I)*  
*\*I.R.T.E.N. Institut de Recherches et de Traitement Statistique pour les*

*Elements Naturels, Loubens, Lauragais*

*\*\*Dipartimento di Scienze Cliniche e Biologiche, Università di Torino (I)*

*\*\*Crac/Toulouse Centre Claudius Regaud (F)*

## INTRODUCTION

Recent research lead in a interdisciplinary way, in our institutes, has shown a possible antiproliferative action of metals and metalloids (iron, boron, zinc), if made to penetrate the cell.

Fructose is used as a means through which trace-elements are bound by carbon to cross the plasmatic membrane of the cell. During this passage an energy is liberated, in the form of UV rays or infrared rays.

At this time it is well known that proteins, hormones, enzymes, have to be activated to take part in the chemical reaction of the metabolism. This means that their molecules must pass to higher level of energy, and this passage is possible through a change in the atomic orbit of their most external electrons.

Metals and or metalloids can activate an organic compound binding themselves to his receptors. This link liberates enough energy to change the electronic arrangement of the molecules which constitute it, leading them to a higher energy

level, and activating a definitive chemical reaction. With this mechanism the trace-elements act as catalyst in the majority of biological reactions. In addition, the metal ions that penetrate into the neoplastic cell cause, through a liberation of quantum energy, a lipidic peroxidation and, consequently, a cellular death. In one of our last studies we tested the action *in vitro* of iron carbonyl (Fe<sup>+++</sup> bound to C6 fructose) and the zinc carbonyl (Zn<sup>++</sup> C6 fructose). This research showed that only the 10% of cancer cells survived after 72 hours of incubation with Fe-FLNT4 and Zn-FLNT4 with a concentration of 100-200 mg/l. From our studies we also noted that it is possible to correlate the exaggerated urinary dispersion of one or more metal ions with specific neoplasia or with their secondary localization. If there are bony or cerebral metastasis for example, the urinary excretion of boron increases; during all cases with a decrease of immunological defenses, we have a greater elimination of lanthanide. This is an indication of cellular destruction. Metals and metalloids introduced can play a fundamental role both in the catalysis of metabolic reactions, and in the repairing mechanism of nucleic acid, as well as in the cytolytic of neoplastic and viral cells.

## MATERIALS AND METHODS

We examined 40 patients, 25 women and 15 men. The age of men is between 23 and 84 years old, the age of women between 32 years and 75 years old.

The patients have been divided for pathology:

Bladder cancer  
Gastric cancer  
Kidney cancer  
Breast cancer  
Bronchial cancer  
Lymphoepithelium of rhynopharynx kind Regaud  
Larynx cancer  
Chronic lymphatic leukemia  
Chronic myeloid leukemia  
Pulmonary cancer  
Cardios of little pelvis  
Thyroid follicular cancer  
NonHodking lymphoma  
Timoma  
Uterine cancer  
Colon cancer  
Leg cancer

In all the cases the diagnosis was recent, except a pulmonary cancer and thyroid follicular cancer, diagnosed in 1977 (see table 1).

The patients have been checked before the treatment, and than every 4 month, with the Atomic Urinary Metallogramm (AUM).

We used the following solutions:

- Boron: containing boron carbonyl
- Iron: containing iron carbonyl
- Zinc: containing zinc carbonyl
- Vanadium: containing vanadium carbonyl

N.B.: The concentration is variable according to the square meter of corporal surface, but the antineoplastic action exerted by the trace-elements, is not dose dependent.

The p  
peroxi  
to the

1) Th  
defici  
Atomic  
2) A  
correl  
higher  
follow  
respec  
consid

## RESUL

PERCENT  
RC + R  
RC + R  
RC = 1  
RP = 5  
NC = 1  
P = 8

LEGEND  
RC = C  
RP = P  
NC = A  
P = P

## GAS

0

13



The products containing metals and metalloids, able to peroxide and than destroy the neoplastic cell, have been given to the patients, according to the following considerations:

- 1) The result of the urinary atomic metallogramm and the deficiencies of macro, and or, trace-elements shown by the Atomic Urinary Metallogramm (AUM);
- 2) A kind of pathology. As mentioned above, positive correlation between the arising of bony metastasis and a higher dispersion of Boron seems impossible. We report, as follows, the pathologies tested during our study and the respective experimental treatment according to the two last considerations (kind of cancer and urinary dispersion).

## RESULTS

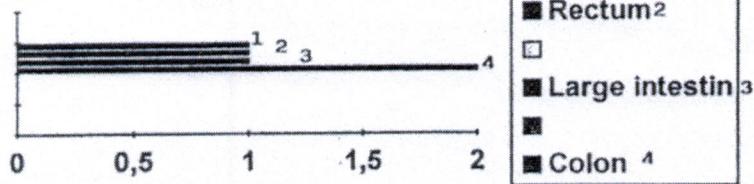
### PERCENTAGE:

RC + RP + NC + P = 40 = 100 %
RC + RP + NC = 32 = 80 %
RC = 11 = 27,5%
RP = 5 = 12,5%
NC = 16 = 40 %
P = 8 = 20 %

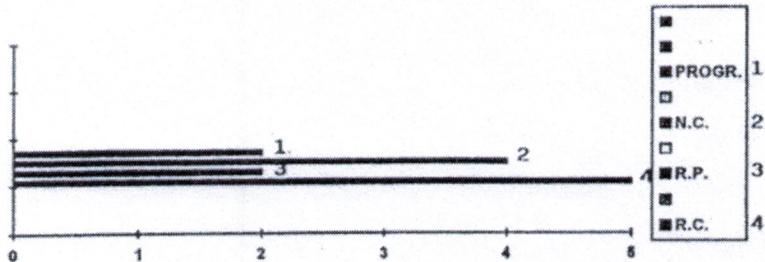
### LEGEND:

- RC = Complete reply
- RP = Partial reply
- NC = Any change
- P = Progression

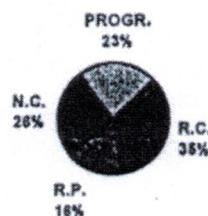
### GASTRIC CANCER WITH CARBONIL THERAPY



### 13 BREAST CANCER WHIT CARBONIL THERAPY

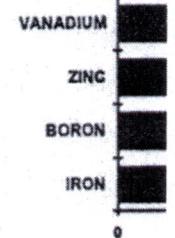


## BREAST CANCER'S TIME REPLY (TEN MOUTH)



KIND of CANCER	PATIENT n°	SEX	YEAR DIAGNOSIS	AGE
Bladder	1	m	'1990	74
Gastric	1	f	1986	71
Kidney	2	m	1985/1993	71/61
Bronchial	1	m	1991	51
Rhynopharinx	1	m	1993	72
L.C.L.	1	m	1992	70
Pulmonary	3	m, m, f	1977/1993/1993	71/49/71
Sarcoma Cartilaginous	1	m	1986	43
Larynx	1	m	1991	84
Thyroid	1	f	1977	75
N.H.L.	1	f	1990	47
Timoma	1	f	1987	32
Uterus	1	f	1993	58
M.C.L.	1	f	1992	46
Sarcoma	1	f	1991	70
Prostatit	2	m	1988/1989	64/80
Melanoma	2	f	1989/1993	66/46
Mesotelioma	1	f	1992	50
Rectum	1	m	1993	64
Large intestine	1	m	1992	68
Colon	2	f/m	1993	60/70
Breast	13	f	1989	63
			1993	63
			1992	67
			1992	38
			1993	38
			1992	75
			1985	78
			1980	64
			1989	57
			1989	62
			1991	45
			1993	44
			1979	50

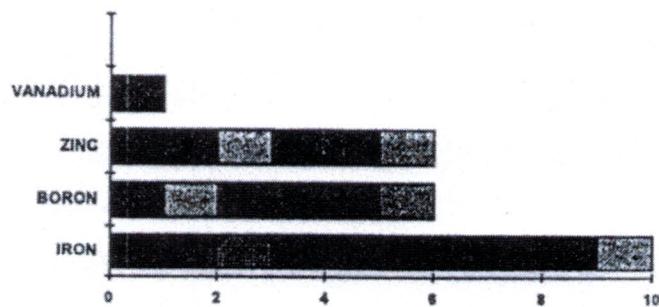
The patient's age is relative to year 1994



### KIND of CANCER

Bladder
Gastric
Kidney
Rhynopharinx
Pharynx
Pulmonary
Larynx
Thyroid
N.H.L.
Bronchial
Timoma
Uterus
M.C.L.
Sarcoma
Prostatite
Melanoma
Mesotelioma
Rectum
Large intestine
Colon
Breast

### PERCENTUAL USING CARBONYL



XVI International  
Cancer Congress  
1994

New Delhi, India  
30 Oct. - 5 Nov. 1994

#### AGE

	KIND of CANCER	PATIENT n°	STAGE	ISTOTYPE
74				
71				
71/61	Bladder	1	pT3N1Mx	PAPILLAR
51	Gastric	1	pT1NoMx	ADENOK
72	Kidney	2	pT2NoMX	ADENOK
70			pT4N2Mo	ADENOK
71/49/71	Rhynopharynx	1	pT1NoMx	ADENOK
43	Pharynx	1	pT3N2Mx	EPIDERMOID
84	Pulmonary	3	pT3N1Mx	ADENOK
75			pT3N2Mx	ADENOK
47			pT2NoMx	ALVEOLAR BRONCH.
32	Larynx	1	pT3NoMx	EPIDERMOID
58	Thyroid	1	T1NoMo	FOLLICULAR
46	N.H.L	1	B	LINF.
70	Bronchial	1	pT1NoMx	EPIDERMOID
64/80	Timoma	1	pT1NoMx	LYMPHOEPITHELIAL
66/46	Uterus	1	T1abNoMo	ADENOK
50	M.C.L.	1	L3	
64	Sarcoma	2	pT2NoMx	SARCOMA
68			pT3NoMx	CARTILAGINEUS
60/70	Prostatite	2	pT2NoMx	ADENOK
63			pT3N2Mx	ADENOK
63	Melanoma	2	2° CLARK	
67			3° CLARK	
38	Mesotelioma	1	pT1NoMo	
38	Rectum	1	pT2NoMo	ADENOK
75	Large intestine	1	pT3N1Mo	ADENOK
78	Colon	2	pT3N2Mx	ADENOK
64	Breast	13	pT2N1Mo	ADENOK
57			pT1NoMo	ADENOK
62			pT1NoMo	ADENOK
45			pT3N1M1	ADENOK
44			pT2N1iiiiMo	ADENOK
50			pT4N2M1	ADENOK
			pT4N2M1	ADENOK
			T1MoMo	ADENOK
			T2N1Mo	ADENOK
			T2NoMo	ADENOK
			T4N2M1	ADENOK
			pTxNoMo	ADENOK
			T2N1Mo	ADENOK

New Delhi, India  
30 Oct. - 5 Nov. 1994

KIND	THERAPY	PT	DATE BEGINN.	QC ALLA DGN	EVOLUTION
Bladder	IRON	1	9/1993	mts O	3/1994 R.C.
Gastric	IRON	1	7/1993	mts ln	11/1993 R.C.
Kidney	IRON	1	5/1993	mts O	10/1993 N.C.
	ZINC-BORON	1	6/1993	mts O	4/1994 PROGR
Rhynopharynx		1			
Pharynx	IRON	1	6/1993	mts O	3/1994 N.C.
L.C.L.	ZINC	1	12/1993	wbc 55000 Wbc 5600	3/1994 + R.C.
Pulmonary	ZINC	1	2/1993	mts O	2/1994 N.C.
	IRON	1	5/1993	mts O	1/1994 BONY
	ZINC	1	10/1993	mts O	3/1994 R.P.
	BORON		1/1994	mts O	4/1994 N.C.
Larynx	BORON ZINC	1	2/1994	mts O	4/1994 N.C.
Thyroid	IRON	1	6/1993	mts O	2/1994 N.C.
N.H.L.	IRON	1	9/1993	recid. 92	3/1994
	ZINC	1	2/1994		mts linf.
Timoma	IRON	1	6/1993	mts O	3/1994 R.P.
Uterus	IRON BORON	1	7/1993	mts O	3/1994 N.C.
M.C.L.	IRON	1	9/1993	mts O	
	ZINC		3/1994		
Sarcoma	IRON	1	10/1993	mts pulm	4/1994 PROGR.
	ZINC		12/1993		
	ZINC	1	9/1993	mts O	2/1994 N.C.
Prostat.	ZINC	1	11/1993	mts bony	2/1994 N.C.
	IRON	1	7/1993	mts bony	2/1994 N.C.
Melanoma	IRON	2	8/1993	mts O	3/1994 R.C.
			1/1994	mts O	2/1994 N.C.
Rectum	ZINC	1	10/1993	mts O	3/1994 R.C.
Large int.	IRON	1	4/1993	mts rec.	4/1994 R.C.
Colon	ZINC	2	10/1993	mts LN	3/1994 N.C.
	ZINC		10/1993	mts LN Liver	3/1994 R.P.
Breast	ZINC	1	11/1993	mts O rec.cut.	1/1994 R.P.
	BORON-ZINC	1	11/1993	mts O	1/1994 N.C.
	IRON	1	6/1993	mts O	8/1993 R.C.
	ZINC	1	9/1993	mts bony 92	3/1994 PROG
	BORON		2/1994		mts LN RO neg
	IRON	1	1/1994	mts O RO neg	3/1994 R.C.
	VANADIUM		2/1994		mts LN
	IRON	1	7/1993	mts O	1/1994 N.C.
	BORON-IRON	1	11/1993	mts O	5/1994 R.C.
	IRON-ZINC	1	8/1993	mts O recid.	1/1994 R.C.
	IRON	1	12/1993	mts LN	1/1994 N.C.
	IRON	1	10/1993	mts LN	1/1994 N.C.
	ZINC-IRON-BORON	1	5/1993	mts LN+Liver	2/1994 R.P.
	IRON-BORON	1	10/1993	mts O	3/1994 R.C.
	IRON-BORON	1	1/1994	mts Liver Pulm mts Thorax	
				Intestine 88	4/1994 PROG

#### METALLOGRAMM ESTIMATION

The urinary dispersion of macroelements iron, boron, lanthanides, is always followed by an evolutive illness; the test correction is followed by its stabilization or reply. In addition, the stabilization of lanthanide's dispersion is correlated to the normalization of CD4 and NK, indicating the direct relation with the immunological reply.

**CONCLUSIVE D**  
We are, therefor the carbonyls, effects. Their efficac phenomenon. Resonance as a The lectines s be superimpose the biological The atomic resp In cancers, ir cytotoxic activ restauratior polymerase, and the metals a carbonyl.

**BIBLIOGRAPHY**  
GRANDI M., AS COURRIERES P., breast and lug Proceedings of Italy, December

GRANDI M., AS Metallic catio in solid tumo Bangkok, Thaila

LAPALUS P. Toxi Université de Pharmalcoologie.

OLUTION  
94 R.C.  
93 R.C.  
93 N.C.  
4 PROGR  
  
94 N.C.  
94 R.C.  
94 N.C.  
94 BONY  
94 R.P.  
94 N.C.  
94 N.C.  
94 N.C.  
94 linf.  
94 R.P.  
94 N.C.  
4 PROGR.  
4 PROGR.  
4 N.C.  
94 N.C.  
94 N.C.  
94 R.C.  
94 N.C.  
94 R.C.  
94 R.C.  
94 N.C.  
994 R.P.  
994 R.P.  
994 N.C.  
993 R.C.  
994 PROG  
N RO neg  
994 R.C.  
LN  
994 N.C.  
994 R.C.  
994 R.C.  
994 N.C.  
994 N.C.  
994 R.P.  
994 R.C.  
s Thorax  
994 PROG

## CONCLUSIVE DISCUSSION

We are, therefore, in the presence of a new class of drugs: the carbonyls, potentially active, selective, without side effects. Their efficacy is probably correlated to a resonance phenomenon. Resonance as a balance element on lymphocyte underpopulations. The lectines surface of T4 and the spectrum of connection can be superimposed to the spectrum of macrophages according to the biological concept of antigens of hystocompatibility. The atomic response comes before the molecular response. In cancers, iron, zinc, boron and vanadium, are able to have a cytotoxic activity, through a blockage of the membrane and a restauration of the lipidic peroxidation which than block the polymerase, and also the transcriptase by radiative action of the metals associated with the presence of CO radical carbonyl.

## BIBLIOGRAPHY

- GRANDI M., ASSOUN C., MAGGIORA M., NUMICO G., CANUTO R., COURRIERES P., SOULA P. Iron-carbonyle: preliminary results on breast and lung cancer. Advances in management of malignancies. Proceedings of the Third International Congress held in Pisa, Italy, December 6-10, 1993; pagg. 267-269. Editoriale Bios.
- GRANDI M., ASSOUN M., ASSOUN C., NUMICO G., DI PALMA A. Metallic cations as illness markers and therapeutic proposal in solid tumors. The 11th Asia Pacific Cancer Conference, Bangkok, Thailand, November 16-19, 1993.
- LAPALUS P. Toxicité aigue des 8 préparations métalliques. Université de Nice. Faculté de Médecine. Laboratoire de Pharmacologie.

XVI International  
Cancer Congress  
1994

New Delhi, India  
30 Oct. - 5 Nov. 1994

boron,  
ss; the  
ly.  
sion is  
ing the



## XVI INTERNATIONAL CANCER CONGRESS

Oct 30 - Nov 5 1994 New Delhi, India



President  
D.J. Jissawalla  
Vice-President  
Ms. Usha K. Luthra  
Secretary-General  
P.B. Desai  
Joint Secretaries  
M.G. Desai  
R.S. Rao

CONFIDENTIEL

Date : 18/08/94

Dear DR. GRANDI,

This is to inform you that your poster (Ref.No. A-00971) entitled :

PRELIMINARY RESULTS FOR SOME RESPONSES IN CANCERS WITH METAL-CARBONYL COMPOUNDS UNDER ASSOCIATED IMMUNOTHERAPY. METAL-FLNT4 COMPLEX (ZN, FE, V. OTHERS).

is scheduled for presentation on 31/10/94 at Hotel VIGYAN BHAVAN.

You are requested to put up the poster for display in the morning at 8.30 a.m. and be present for the discussion at 16:00 hrs.

Your poster number is PSB11-07. Please quote this number in future correspondence.

With regards,

Sincerely yours,

*Mr*  
R.S. Rao  
*for* Chairperson  
Scientific Programme Committee.

To,  
DR. GRANDI MAURIZIO  
CENTRO STUDI RICERCHE E TERAPIA  
DELLE NEOPLASIE  
"LA TORRE", 10, VIA PONZIO - TORINO  
10141  
ITALY

Congress Secretariat: Tata Memorial Centre, Parel, Bombay 400 012, INDIA.  
Tel.: 91-22 4146605 Ext. 4205/4270, 91 22-4129399 & 91-22-4146536 (Direct) • Telex: 91-11-73649 TMC IN  
Telefax: 91-22-4139318 & 91-22-4146937



fructose-zinc assoun

Rechercher

Environ 44 résultats (0,22 secondes)

Recherche avancée

Tout

Plus

Le Web  
Pages en français  
Pays : Suisse

Plus d'outils

**ZINC DEFICIENCY INCREASES THE DELETERIOUS EFFECT OF HIGH FRUCTOSE ...** [ Traduire cette page ]

de B Lachili - 2002 - Autres articles  
 standard diet but 58% of sugars were fructose, Zn: 64ppm) and fructose zinc deprived group receiving the F diet but zinc deprived (n = 09, Zn: 6ppm, FZD).

...  
[www.springerlink.com/index/m611180m52qup2q7.pdf](http://www.springerlink.com/index/m611180m52qup2q7.pdf)

Liens commerciaux

**Fructose - En vente ici**

Fort pouvoir sucrant pour vos plats  
 Epicerie fine - Frais de port 7.50€  
[www.bienmanger.com](http://www.bienmanger.com)

Affichez votre annonce ici »

**[PDF] METAUX LOURDS TOXIQUES ET DEQUELATIONS**

Format de fichier: PDF/Adobe Acrobat - [Afficher](#)  
 par exemple des formes de zinc associées à une molécule de Fructose ... Christian Daniel ASSOUN ;  
 Président de Glycan Group (Etats-Unis, Espagne,  
 Suisse- ...  
[www.le-silicium-organique.com/store/MetauxLourdsToxiquesDequelandFR](http://www.le-silicium-organique.com/store/MetauxLourdsToxiquesDequelandFR)

**[PDF] PRELIMINARY RESULTS FOR SOME RESPONSES IN CANCERS WITH METAL ...** [ Traduire cette page ]

Format de fichier: PDF/Adobe Acrobat - [Afficher](#)  
 M. GRANDI, C. ASSOUN\*, R.A. CANUTO, P.  
 COURRIERE\*\*, P. SOULA\*\*, M. MAGGIORA\*\*, A.  
 LACIVITA ... fructose) and the zinc carbonyl (Zn++  
 C6 fructose). ...  
[www.le-silicium-organique.com/store/Preliminaryresults.pdf](http://www.le-silicium-organique.com/store/Preliminaryresults.pdf)

Plus de résultats de [www.le-silicium-organique.com](http://www.le-silicium-organique.com)

**Glycan Group - Métallogramme Atomique****Urinaria**

Dr. Christian Daniel ASSOUN, par ailleurs co-fondateur du concept de Médecine .... de Zinc complexée électrochimiquement à une molécule de fructose faisant ...  
[www.glycangroup.com/mau.html](http://www.glycangroup.com/mau.html) -  
 En cache - Pages similaires

**Fibromyalgie**

Dr. Christian Daniel ASSOUN. La fibromyalgie ne possède pas à ce jour une .... Notamment la dépression et la détérioration du pool du Zinc et du ... d'un atome de Zinc complexé de manière électrochimique à une molécule de Fructose. ...  
[www.glycangroup.com/group/index.php?...9...](http://www.glycangroup.com/group/index.php?...9...) -  
 En cache

Plus de résultats de [www.glycangroup.com](http://www.glycangroup.com)

**[PDF] CADMIUM RESISTANCE OF APPLE ROOTSTOCKS M.9 AND B.396 IN VITRO** [ Traduire cette page ]

Format de fichier: PDF/Adobe Acrobat - [Afficher](#)  
 de J SAKALAUSKAITÉ - Autres articles  
 induced accumulation of fructose and sucrose in the leaves of both rootstocks. .... and zinc in white beans // Can J Bot 1978. Vol. 56. P.1744-1749. ... St ohs S. J., Bagchi D., Hassoun E., Bagchi M. ...

[www.lsdi.lt/straipsniai/25-3/25\(3\)-37.pdf](http://www.lsdi.lt/straipsniai/25-3/25(3)-37.pdf) -  
Pages similaires

### Hépatopathies métaboliques congénitales —

#### Recommandations pour la ...

de G Touati - 1999 - Autres articles

... Eliane Depondt 2, Murielle Assoun 2 and Jean-Marie Saudubray 1 .... Il doit évaluer s'il y a prise de galactose ou de fructose, l'importance de la prise de ..... L'administration de zinc par voie orale a également recommandé. ...  
[linkinghub.elsevier.com/retrieve/pii/S0985056299800569](http://linkinghub.elsevier.com/retrieve/pii/S0985056299800569)  
- Pages similaires

### Preliminary Results for some responses in

#### cancers ... - [ Traduire cette page ]

In one of our last studies we tested the action in vitro of iron carbonyl (Fe+++ bound to C6 fructose) and the zinc carbonyl (Zn++ C6 fructose). ...  
[www.glycanlab.com/index.php?option=com...](http://www.glycanlab.com/index.php?option=com...) -  
En cache

### Petites annonces gratuites - de Bretagne

#### Coup de Coeur ?- Coup de ...

Le M.A.U a été mis au point par le Professeur Christian Daniel ASSOUN (co-fondateur de ... de Zinc complexée électrochimiquement à une molécule de fructose. ...  
[www.senpaga.fr/detail22\\_tribune-libre-avis-opinions\\_cancers-autres-maux-du-corps\\_3572786](http://www.senpaga.fr/detail22_tribune-libre-avis-opinions_cancers-autres-maux-du-corps_3572786) -  
En cache

### [PDF] Phénylcétonurie

Format de fichier: PDF/Adobe Acrobat - Version HTML  
minéraux et oligoéléments (vitamine B12, zinc, sélénium) qui .... Mme Murielle Assoun, centre de formation au traitement à domicile ...  
[www.orpha.net/data/patho/Pro/fr/PNDS\\_Phenylcetonurie.pdf](http://www.orpha.net/data/patho/Pro/fr/PNDS_Phenylcetonurie.pdf)

1 2 3

Suivant

fructose-zinc assoun	Rechercher
----------------------	------------

[Rechercher dans ces résultats](#)

[Conseils de recherche](#)

[Envoyez-nous vos commentaires](#)

[Accueil Google](#)   [Programmes de publicité](#)   [Confidentialité](#)   [À propos de Google](#)

# XVI INTERNATIONAL CANCER CONGRESS 1994

New Delhi (India), October 30 - November 5, 1994

Full Name

PROF. MAURIZIO GRANDI

"LA TORRE" Centro Studi Ricerche e Terapia delle  
Neoplasie.

(Address)

VIA PONZIO 10 - 10141 TORINO - ITALIA

941030

I herewith authorize for publication in the Proceedings of the Free Papers and Posters of the aforementioned Congress the paper entitled:

Preliminary results for some responses in cancers with METAL - Carbonyl compounds

(use upper-case letters only where necessary)

under associated immunotherapy. METAL - FLNT4 complex (ZN,Fe,V. others).

by the Authors (first name initial, full surname)

1° M. GRANDI

"LA TORRE" Centro Studi Ricerche e Terapia delle Neoplasie(TO)

C. ASSOUN

(full name of Institute) Institut de Recherches et de Traitement (L'OBENS  
I.R.T.E.N.) Statistique pour les Elements Naturels. LAURAGAIS

2° R.ACANUTO

(full name of Institute) Dipartimento di Scienze Cliniche e Biologiche Università  
di Torino (TO)

3°

(full name of Institute)

CRAC / TOULOUSE CENTRE CLAUDIUS REGAUD

4° P. COURRIERE

(full name of Institute)

CRAC / TOULOUSE CENTRE CLAUDIUS REGAUD

5° P. SOULA

(full name of Institute)

Dipartimento di SCienze Cliniche e Biologiche UNiversità Torino

6° M. MAGGIORA

(full name of Institute)

"LA TORRE" Centro Studi Ricerche e Terapia delle Neoplasie

others A. LACIVITA

(full name of Institute)

TORINO

M. Grandi, C. Assoun, M. Maggiora, G. Numico  
R. Canuto, P. Courriere, P. Soula

Iron-carbonyl: preliminary results on breast and lung cancer

Estratto

# ADVANCES IN MANAGEMENT OF MALIGNANCIES



Edited by  
ANGELO CARPI • ANDREA SAGRIPANTI • BRUNO GRASSI

Co-editor  
GUIDO LUZZATTI

Proceedings of the Third International Congress  
held in Pisa, Italy, December 6-10, 1993



EDITORIALE BIOS



UNIVERSITÀ DEGLI STUDI DI PISA  
Third International  
Congress

**ADVANCES IN  
MANAGEMENT OF  
MALIGNANCIES**

Edited by

A. Carpi, A. Sagripanti,  
B. Grassi  
Pisa, Italy  
December 6-10, 1993

## **Iron-carbonyl: preliminary results on breast and lung cancer**

\*M. Grandi, °C. Assoun, \*\*M. Maggiora,

\*G. Numico, \*\*R. Canuto, \*\*\*P. Courriere,  
P. Soula\*\*\*

\* Centro Studi Ricerche e Terapia delle Neoplasie, Torino

\*\* Dipartimento di Medicina ed Oncologia Sperimentale  
Università di Torino

°I.R.T.E.N. France - En Bousquet 31460 Loubens Lauragais

\*\*\* CRAC/Toulouse

### **INTRODUCTION**

The recent studies have showed the antiproliferative activity of the carbonyl group with an insaturation in  $\alpha-\beta$  position of carbonic chain which is tied up to. From this chemical group would depend, in fact, the action of some eicosanoids against neoplastic cells.

We are from a long time evaluating in vitro activity of some compounds, such as, metallic ions, for their properties to induce the lipidic peroxidation in the neoplastic cell.

Our group is considering the use of ferric ions tied up to the carbonyl group, obtained from the fructose molecule against some lines of animals and humans neoplastic cells at different degree of deviation.

A fructose iron and zinc has been employed. It's a Fe<sup>3+</sup> and Zn<sup>2+</sup> fixed complex in presence of hemicycle structure in C6.

### **MATERIALS AND METHODS**

We tested Fe-Carbonyl with two cellular lines of human cancers in culture: the MCF7 (from a breast adenocarcinoma) and the A549 (from lung cytotoxicity carcinoma) using, as test, a non clogenic assay, which consists in dyeing of intracellular proteins from the Sulforodamina B.

Yoshida ascites AH-130 hepatoma cells were maintained i.p. in rats and transplanted through serial passages carried out at 7-day intervals. Six-day-old hepatoma cells were collected in a sterile way from animals, separated from the ascitic fluid, and resuspended in RPMI 1640 medium with 1% bovine serum albumin and new born calf serum (10%) so as to have  $20 \times 10^6$  cells/10 ml. Various concentrations of Fe-FLNT4 or Zn-FNLT4 were added to cell suspension, and after 1 h. and 21 h. of incubation at 37° C, the number and the viability of the cells were determined.

To obtain a comparison high deviation cellular line we tested the Fe-FLNT4 and the Zn-FLNT4 on the AH-130 line.

## RESULTS

The results A549 and MCF lines are similar. Only the 9-10% of cells survive after 24-72 hours of incubation with Fe-FLNT4 and Zn-FLNT4 at concentrations of 100-200 mg/l. The increase of concentrations does not seem to increase cytostatic activity of the compound.

As show in table 1 and 2, the cells do not grow in the presence of 43 mg/l Zn-FLNT4 and 142 mg/l Fe-FLNT4. The viability is also affected by same concentrations of the substances (table 3 and 4).

Number of hepatoma cells ( $\times 10^6/\text{ml}$ ) after treatment with Zn-FLNT4				
Time	Zn 21.5 mg/l	Zn 43 mg/l	Zn 86 mg/l	Zn 172/l
0 h	1.500 = 0.000			
4 h		1.100	1.612	1.633 = 0.213
24 h		1.525	1.587	1.808 = 0.569
				2.150
				1.725

Table 1

Number of hepatoma cells ( $\times 10^6/\text{ml}$ ) after treatment with Fe-FLNT4				
Time	Control	Fe 71 mg/l	Fe 142 mg/l	Fe 284 mg/l
0 h	1.500 = 0.000			
4 h	1.908 = 0.014	1.837	1.742 = 0.191	1.737
24 h	2.608 = 0.088	1.825	1.500 = 0.319	1.675

Table 2

Viability of hepatoma cells treated with Fe-FLNT4				
Time	Control	Fe 71 mg/l	Fe 142 mg/l	Fe 284 mg/l
4 h	94.56 = 1.78	92.99	93.22 = 1.67	92.41
24 h	85.45 = 5.51	47.54	24.13 = 1.47	58.07

Table 3

Viability of hepatoma cells treated with Zn-FLNT4				
Time	Zn 21.5 mg/l	Zn 43 mg/l	Zn 86 mg/l	Zn 172 mg/l
4 h	90.36	93.27	92.53 = 1.13	93.78
24 h	31.18	30.32	60.19 = 5.52	80.46

Table 4

At 4 h of incubation, the hepatoma cell viability is not decreased while the cell growth is already a little affected.

It is important to consider the concentrations of the substances. In fact the highest concentrations decrease less the cell viability.

The viability of the cells was determined by lactate dehydrogenase activity present in the hepatoma cells after incubation with Fe or Zn and data, means of 2 or 3 experiments, are expressed as percentage of total activity present in the cells before incubation.

The control is the same for cells treated with Fe or Zn. Yoshida ascites Ah-130 hepatoma cells were incubated  $1.5 \times 10^6$ /ml.

### CONCLUSIONS

The FLNT4 action mechanism is not known until now. For the first hypothesis is possible to affirm that could act on cell surface influencing the mechanism of transmembrane active transport.

The resulting effect on the membrane would be the stiffening lipidic bilayer, with the block of the surface lectins and of the inside-outside active transport.

The surface glycoproteins can be break up by the constitution of carbonyl-group tied up to some metals, the cytotoxicity difference (dependent-cycle) between ZnFLNT4 and FeFLNT4 suggest the hypothesis both structural (membrane's protein) and genetic (inhibited polymerase) by Zn<sup>2+</sup> and Fe<sup>3+</sup> associated to C = O.

The radiative properties giving ZnII, FeII, being different (spectral distribution UV), the protonic flux of ATP synthetase membrane's in presence of ZnFLNT4 and FeFLNT4 grant a privilege, an inside perturbation in the protein synthesis but at the same time, outside the cancer cell; a block of surface lectins, the membrane's cytoskeleton rigidity can be the result of a dehydratation to Schiff bases or some Amadori products (terminal glycosylation).

These hypothesis might be verify by electronic microscopy.

These mechanisms, as they will be completely explained, will show the setting up of selective antimitotic agents of malignant cells and weakly cytotoxic for T4 cells.

**Address for correspondence:**

Prof. Maurizio Grandi  
P.zza Rivoli, 11  
I - 10139 Torino - Italy