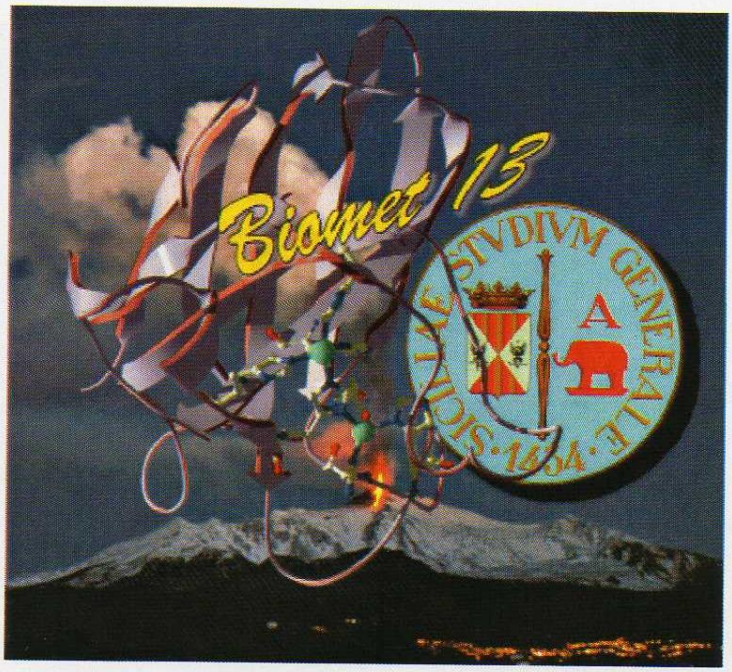

Thirteenth workshop on PharmacoBioMetallics

Biomet13

BOOK OF ABSTRACTS

Camplus D'Aragona, Via Monsignor Ventimiglia, 184 – Catania

25 – 26 Ottobre 2013

Organizzato da:
Unità locale dell'Università degli Studi di Catania
per il
Consorzio Interuniversitario di Ricerca in Chimica dei metalli nei Sistemi Biologici
(C.I.R.C.M.S.B.)

Dibuthyltin(IV) Complexes with Caffeic acid: Apoptotic Effect on human cancer cells

Claudia Pellerito,[1] Ornella Morana,[1] Cristina Prinzivalli,[1] Tiziana Fiore,[1] Antonietta Notaro,[2] Selenia Sabella,[2] Giuseppe Calvaruso.[2]

[1]*Dipartimento di Fisica e Chimica, Università degli Studi di Palermo Viale delle Scienze, Parco d'Orleans, Ed. 17 - 90128 Palermo*
[2]*Dipartimento di Scienze e Tecnologie Biologiche, Chimiche e Farmaceutiche (STEBICEF) Università degli Studi di Palermo, Plesso di Biochimica, Policlinico,Via del Vespro, 129 - 90127 Palermo*

Some naturally occurring phenolic acids and analogues, such as caffeic and gallic acids, are known to display a wide variety of biological functions, in addition to their primary antioxidant activity, which are mainly related to modulation of carcinogenesis.[1,2] Indeed, many phenolic compounds have been investigated for their potential use as cancer chemopreventive agents.[3] Caffeic acid and chlorogenic acid exhibit antioxidant activity *in vitro*. and have been shown to have multiple pharmacological properties including anti-inflammatory, antimetastatic, antitumorigenic and inhibition of HIV replication.[4] Further, several studies have identified caffeic acid to be an inducer of apoptosis in cancer cell lines and capable of tumor growth inhibition and regression in animals.[5,6]

The biological activities of the catechins have been reported to be influenced by metal ions, especially by transition metal ions.[7]

Caffeic acid (H_3CAF) possesses two possible chelating sites in competition: the catechol (*ortho*-dihydroxybenzene) and the carboxylic acid functions. These two functions are the major ligands of humic substances able to coordinate metal ions.

This work deals with the synthesis, the chemical characterization of the newly synthesized potential anti-tumor dibutyltin(IV) complexes containing caffeic acid ligand [$Bu_2Sn(IV)HCAF$], and the individuation of possible specific cytotoxic action on tumor cells. The coordination environment at the tin center was investigated spectroscopically through a series of techniques, both in solid and solution phases. The present study concentrates on the evaluation of the growth inhibition and cytotoxic activity of $Bu_2Sn(IV)HCAF$ towards a human cancer cell lines (HCT116 colorectal cancer, MDA-MB-231 breast cancer and HepG2 hepatocarcinoma). Caffeic acid and precursor dibutyltin(IV) chloride (Bu_2SnCl_2) were also considered for comparison. The effect of a variation in structure of $Bu_2Sn(IV)HCAF$ found to lead to a clear change in the respective antiproliferative properties: $Bu_2Sn(IV)HCAF$ induces loss of viability in HCT116, MDA-MB-231, HepG2; moreover, the complex shows only moderate effects in non-tumor Chang liver cells. $Bu_2Sn(IV)HCAF$ exerts lower cytotoxic activity than Bu_2SnCl_2, suggesting that the binding with caffeic acid modulates the marked cytotoxic activity exerted by Bu_2SnCl_2; $Bu_2Sn(IV)HCAF$ displays a considerably more pronounced antitumoural effect towards both cell lines than caffeic acid. We also demonstrated that cytotoxic activity was associated with the induction of apoptosis.

Bibliografia
1. Rao, C.V.; Desai, D.; Rivenson, A.; Simi, B.; Amin, S.; Reddy, B.S. Cancer Res. 55 (1995) 2310.
2. Leu, T.H.; Maa, M.C. Curr. Med. Chem. Anti-Canc. Agents. 2 (2002) 357.
3. Tapiero, H.; Tew, K.D.; Ba, G.N.; Mathe, G. Biomed. Pharmacother. 56 (2002) 200.
4. Bhat, S.H.; Azmi, A.S.; Hadi, S.M. Toxicology and Applied Pharmacology, 218 (2007) 249
5. Chung, T.W.; Moon, S.K.; Chang, Y.C.; Ko, J.H.; Lee, Y.C.; Cho, G.; Kim, S.H.; Kim, J.G.; Kim, C.H. FASEB J. 18 (2004) 1670.
6. Orsolic, N.; Knezevic, A.H.; Sver, L.; Terzic S.; Basic, I. J. Ethnopharmacol. 94 (2004) 307.
7. Furukawa, A.; Oikawa, S.; Murata, M.; Hiraku, Y.; Kawanishi, S. Biochem. Pharmacol. 66 (2003) 1769.