World Research Journal of Applied Medicinal Chemistry
ISSN: 2230-9314 & E-ISSN: 2230-9322, Volume 1, Issue 2, 2011, PP-28-31
Online available at http://www.bioinfo.in/contents.php?id=64

BIOLOGICAL STUDIES OF SOME NEW ORGANOTIN (IV) DERIVATIVES OF 3, 4-METHYLENEDIOXY-6-NITROPHENYLPROPENOIC ACID

RANI SUSHMA[1], TEWARI I.C.*[2]
[1]Department of Chemistry, D.G. (P.G.) College, Kanpur, India
[2]Department of Chemistry, D.B.S. (P.G.) College, Kanpur, India
*Corresponding Author: Email- drictewari@gmail.com

Received: November 15, 2011; Accepted: December 03, 2011

Abstract- The present manuscript describes the biological studies of some organotin(IV)derivatives of 3,4-methylenedioxy-6-nitrophenylpropenoic acid which are synthesized and characterized by standard methods and tested for their antibacterial activity against pathogenic bacterial strains *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Klebsiela pneumoniae*; antifungal activity against *Aspergillus flavus* and *Aspergillus niger* and antitumor activity against human breast adenocarcinoma(MCF-7) and mammary cancer cell (EVSA-7) lines in-vitro and results indicates that these compounds are potentially active in biological screening.

Introduction

There is an enormous potential of metals in medicines and their selection offers the possibility for the discovery of new metallodrugs [1-3]. The chemotherapeutic values of organotin compounds have been expanded as they have found their place among a class of potential biologically active compounds exhibiting antimicrobial activity against different kinds of microbial strains [4-14]. They also show anti-inflammatory and cardiovascular activity [15], trypanosomal activity [16,17] along with anti-herpes [18] and anti-tubercular activity [19]. It was found that over the last 30 years, research on chemistry of organometallic compounds of tin in +4 oxidation state has represented one of the most prolific areas of chemical activity. The present manuscript deals the pharmacological screening of newly synthesized organotin compounds against pathogenic bacterial strains *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Klebsiela pneumoniae*; antifungal activity against *Aspergillus flavus* and *Aspergillus niger* and antitumor activity against human breast adenocarcinoma (MCF-7) and mammary cancer cell (EVSA-7) lines in-vitro.

Experimental

The organotin (IV) complex of 3, 4-methylenedioxy-6-nitrophenylpropenoic acid were synthesized by refluxing the stochiometric amount of the ligand acid with corresponding organotin chloride in presence of triethylamine using reported method [20].

Antibacterial Activity

Antibacterial activity of the synthesized organotin compound was carried out by disc diffusion method [21] using ampicilin as standard. The filter paper (Whatmann No.1) sterile disc of 5 mm diameter, impregnated with the test compounds (10 μg/ml of ethanol) along with standard were placed on the nutrient agar plate at 37°C for 24 hrs in BOD incubator. The inhibition zone around the dried impregnated disc was measured after 24 hrs. The activity was classified as highly active (dia = > 15 mm), moderately active (dia = 10-15 mm) and slight active (dia = 5-10 mm). The diameter less than 5 mm was regarded as inactive.

Antifungal Activity

The antifungal activity of the organotin compound was tested by agar plate diffusion method [22], using ampicilin as standard. The two concentrations of the test compounds viz., 50 and 100 μg/ml were prepared and tested against two pathogenic fungal strains, *Aspergillus flavus* and *Aspergillus nigar*. The one ml of each compound was poured into a Petri dish containing 20-25 ml of molten potato dextrose-agar medium. As the medium solidify, Petri dishes were inoculated at 37°C for 96 hrs in BOD incubator. After 96 hrs the colony diameter was measured and % inhibition was calculated using standard method.

Antitumor Activity

The *in-vitro* antitumor activity of these compounds was carried out by MTT-Method [23]. This method was performed to estimate the effect of compounds on the growth of cell. The human breast adenocarcinoma (MCF-7) and mammary cancer (EVSA-7) cell lines were used for this purpose. The principle behind this assay depends upon the reduction of tetrazoleum salt. The yellow colored tetrazoleum MTT [3-(4, 5-dimethylthiazolyl-2)-2, 5-diphenyl tetrazoleum bromide] was reduced partially by metabolically active cells by the action of dehydrogenase enzyme to generate NADH and NADPH as reducing equivalents. The resulting

intracellular purple Colour zone was solubilized and quantified by spectrophotometer. The MTT was first dissolved in Phosphate buffer saline at a concentration of 5 mg/ml. The MTT solution (50 μl) was added to each well of 96 well culture plate containing 100 μl of culture medium and incubates at 37°C for 4 hrs. The medium was then removed carefully without disturbing the crystals of purple colored zone. 50 ml of DMSO was then added to each well and mixed thoroughly to dissolve the crystals of the zone. The plate was then read on a micro ELISA plate reader at a wavelength of 570 nm to find out the optical density and cell count value.

Results and Discussion

All the newly synthesized compounds are crystalline solids. They are air stable and soluble in common organic solvents. The compounds were further characterized by using various analytical techniques such as elemental analysis, infrared spectroscopy, multinuclear NMR and mass spectrometry, in order to ascertain their structures and explore other properties.

Antibacterial Activity

These organotin carboxylates were tested for antibacterial activity against three bacterial strains viz. *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Klebsiela pneumoniae* using 10 μg/ml concentration of test compound. These compounds show higher to moderate activity against these bacterial strains. It was found that these compounds may generally form complexes with metaloenzymes, particularly those which responsible in basic physiology of a cell such as *cytochrome oxidase*. These compounds may interacted with peptidoglycan layer of bacterial cell wall and damage it by penetrating in such a manner that the ligand/carboxylate group gets entered inside the bacterial cell wall by puncturing it followed by damage of bacterial cell. Some times these compounds in low concentration may cause bacteriostatic condition by slow down the growth of bacterial cells.

Antifungal Activity

These organotin carboxylates were also tested for their fungicidal activity against the two pathogenic fungal strains *Aspergillus flavus* and *Aspergillus nigar* using different concentrations viz. 50 and 100 μg/ml. It may be observed that the efficacy of these compounds against fungal strains was variable. At low concentration the efficacy was less against fungal strains while at higher concentration all these compounds show higher efficacy. The variation in activity was due to presence of different carboxylates groups as ligands.

***In-vitro* Antitumor Activity**

Antitumor activity of these organotin compounds was studied against the human breast adenocarcinoma (MCF-7) and mammary cancer (EVSA-7) cell lines *in-vitro*. These compounds show moderate activity against these two tumor cell lines. It was observed that the variation in efficacy of these compounds may be presence of different ligand/ carboxylic group in the compound. These compounds generally interact with the receptor site of enzyme complexes which are responsible for the cytostatic and cytotoxic conditions for cell. It may be noted that these organotin compounds generally interacted with purine bases in DNA molecule, where they reacted with labile hydrogen present on N-7 position and form complex with DNA strands by interrupting the replication and transcription process inside the DNA molecule and stop the cell division along with protein synthesis.

Conclusion

The above discussion of results clearly indicates that these organotin compounds show better results against tumor cell lines *in-vitro* along with bacterial and fungal strains. These compounds would be treated as drugs in future for the treatment of such kinds of diseases.

References

[1] Bishayee A., Karmaker R., Mandal A., Kundu S.N., Chaterjee M. (1997) *Eur. J. Cancer. Prev*., 6, 58-70.

[2] Chakraborty A., Chaterjee M. (1994) *Neoplasma*, 41, 291-296.

[3] Cruz T.F., Morgon A., Min W. (1995) *Mol. Biochem*., 153, 161-166.

[4] Barbieri R., Huber F., Silvestru C., Ruisi G., Roosi M., Barone G., Paulsen A. (1999) *Appl. Organomet. Chem*., 13, 595.

[5] Nath Mala, Yadav Rakesh, Eng. G., Nguyen T.T., Kumar Ashok (1999) *J. Organomet.Chem*., 577(1), 1-8.

[6] Faure R., Vincent M., Dufour M., Shaver A., Posner B. I. (1995) *J. Cell. Biochem*., 389-401.

[7] Kuo Y.L., Liu A.H., Marks T.J. (1995) *Metal ions in biological systems, New York, Marcel, Decker*, 53-85.

[8] Hart M.M., Adamson R.H. (1971) *Proc. Natl. Acad. Sci. USA*, 68, 1623-1626.

[9] Hart M.M., Smith C.F., Yancey S.T. (1971) *J. Natl. Cancer Inst*., 47, 1121-1127.

[10] Edwards C.L., Hayes R.L. (1969) *J. Nucl. Med*., 10, 103-105.

[11] Chitamber C.R., Boon P., Wereley J.P. (1996) *Clin. Cancer Res*., 2, 1009-1015.

[12] Wang F., Jiang X., Yang D.C. (2000) Anti-*Cancer Res*., 20, 799-808.

[13] Desoize B., Keppler B.K., Akeli M.G., Etienne J.C., Collery P. (2000) *Metal ions in biology and medicine,* 6, 573-576.

[14] Collery P., Lechinault F., Cazabat A. (2000) *Anti. Cancer. Res*., 20, 955-958.

[15] Chitamber C.R., Wereley J.P. (1997) *J. Biol. Chem.*, 272, 12151-12157.

[16] Hata Y., Sadler A., Lochrer P.J. (1994) *Oncol. Res*., 6, 19024.

[17] Collery P., Millart H., Pluot M., Anghileri L.J. (1986) *Anticancer. Res*., 6, 1085-1088.

[18] Collery P., Anghileri L.J., Morel M., Tran G., Rinjard P., Etienne J.C. (1992) *Metal ions in biology and medicine*, 2, 176-177.
[19] Tajmir-Riahi H.A., Naqvi M., Ahmad R. (1990) *Toxicol. Appl. Pharmacol*, 106, 462-468.
[20] Shukla Shailendra K., Tiwari V. K., Rani Sushma, Kant Ravi, Tewari I.C. (2011) *Inter. Jour. Agri. Sci.,* 3(3), 121-127.
[21] Verma R.S., Imam S.A. (1973) *Ind. J. Microbial*, 13, 45.
[22] Tiwari V.K., Shukla Shailendra K., Chauhan V. S., Kant Ravi, Rani Sushma, Tewari I.C. (2010) *Inter. Jour. Pharma. Analy.* 2(1), 09-14.
[23] Shukla S.K., Tiwari V.K., Chauhan V.S., Rani Sushma, Singh R.K., Kant Ravi, Tewari I.C. (2009) *Inter. Jour. Biotech. Reser.* 2(1), 41-45.

Table 1- Physical data of organotin (IV) derivatives of 3, 4-methylenedioxy-6 nitrophenylpropenoic acid

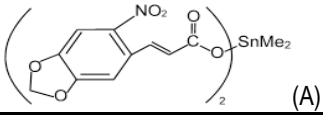
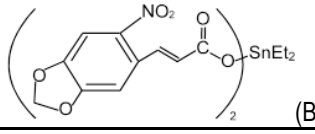
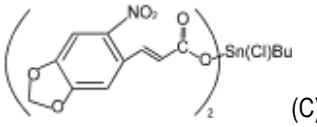
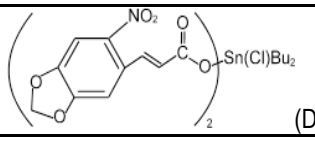
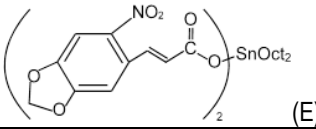
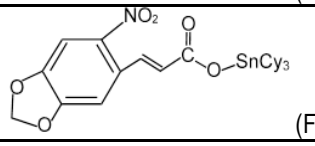
S.N.	Compounds	M.P. (°C)	Yield (%)	Elemental Analysis (%)		
				C	H	N
1	 (A)	237-240	86	42.51	2.9	4.51
2	 (B)	176-178	67	44.35	3.46	4.31
3	 (C)	142-145	70	42.13	3.07	4.1
4	 (D)	196-199	73	47.66	4.26	3.97
5	 (E)	151-153	73	52.88	5.63	3.43
6	 (F)	99-101	83	35.63	6.46	2.32

Table 2- Antibacterial activity of organotin (IV) derivatives of 3, 4-methylenedioxy-6 nitrophenylpropenoic acid

S.N.	Compounds Code	Control	*Pseudomonas aeruginosa*	*Staphylococcus aureus*	*Klebsiela pneumoniae*
1	(A)	–	++	++	++
2	(B)	–	++	++	++
3	(C)	–	+++	++	++
4	(D)	–	++	++	++
5	(E)	–	++	++	+++
6	(F)	–	+++	++	++

+ = 6-10 mm; ++ = 10-14 mm; +++= >14 mm; – = Inactive

Table 3- Antifungal activity of organotin (IV) derivatives of 3, 4-methylenedioxy-6 nitrophenylpropenoic acid at 50 μg/ml concentration

S.N.	Compounds Code	*Aspergillus flavus* Col. Dia. (mm)	%Inhibition	*Aspergillus flavus* Col. Dia. (mm)	%Inhibition
1	(A)	0.7	76.6	0.7	65
2	(B)	0.8	73.3	0.8	60
3	(C)	0.8	73.3	0.8	60
4	(D)	0.7	76.6	0.6	70
5	(E)	0.7	76.6	0.5	75
6	(F)	0.5	83.3	0.4	80
7	Control	3	–	2	–

Table 4- Antifungal activity of organotin (IV) derivatives of 3, 4-methylenedioxy-6 nitrophenylpropenoic acid at 100 μg/ml concentration

S.N.	Compounds Code	*Aspergillus flavus* Col. Dia. (mm)	%Inhibition	*Aspergillus flavus* Col. Dia. (mm)	%Inhibition
1	(A)	0.2	93.3	0.3	75
2	(B)	0.1	96.7	0.2	90
3	(C)	0.2	93.3	0.1	95
4	(D)	0.1	96.7	0.1	95
5	(E)	0.4	86.7	0.2	90
6	(F)	0.2	93.3	0.2	90
7	Control	3	–	2	–

Table 5- Antitumor activity of organotin (IV) derivatives of 3, 4-methylenedioxy-6 nitrophenylpropenoic acid

S.N.	Compounds Code	Cell No. x 10^4 (MCF-7)	Cell No. x 10^4 (EVSA-7)	Activity
1	(A)	9.69±0.92	9.66±0.90	+
2	(B)	11.69 ± 1.02	10.68±1.08	-
3	(C)	11.58±1.02	10.62±1.06	-
4	(D)	9.17 ± 0.87	9.69±0.92	+
5	(E)	9.62±0.52	9.62±0.90	+
6	(F)	9.67 ± 0.54	9.69 ± 0.92	+
7	Negative control	10.21±1.01	10.22±1.01	–
8	Positive control	40.26±3.23	41.23±3.28	–

**Negative Control- Culture Medium only*

***Positive Control- 17 β estradiol*