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BIOMEDICINAL AND GASTROPROTECTIVE STUDIES OF SOME FLUORINE BASED DIORGANOBISMUTH (III) COMPOUNDS

SONI K.K.[1], KUMAR ALOK[1] AND KANT R.[2]*

[1]Department of Chemistry, B.B.D. University, Lucknow, India
[2]Department of Chemistry, Mewar University, Chittorgarh, Rajasthan, India
*Corresponding Author: Email-drrkt78@yahoo.co.in

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Abstract-Some novel bis(pentafluorophenyl)bismuth(III) carboxylates of the type, $R_2Bi(III)L$; where 'R' represent for bis(pentafluorophenyl) group and 'L' represent the corresponding carboxylate ligands were synthesized by the method reported earlier and further characterized by M.P., elemental and I.R., NMR spectral analysis along with their biomedicinal and gastroprotective studies. The antimicrobial studies were carried out against different pathogenic bacterial and fungal strains while the *in-vitro* antitumor activity of these compounds were screened against human breast (MCF-7) and mammary cancer (EVSA-7) cell line. It was found that these compounds have shown potentiality as antitumor and antimicrobial agents. The compounds were also tested for gastroprotective (Anti-ulcer) activity in rats using standard methods and it was found that these compounds exhibit higher activity than the standard ranitidine when the tests were carried out with aspirin (ASP) induced and moderate activity was seen when the tests were done with ethanol (EtOH) induced.

Keywords- Organobismuth, Antimicrobial, Antitumor, gastroprotective.

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Introduction

It is known that there is an enormous potential for the application of metals in medicine [1] and the selection of metal ions offer the possibility for the discovery of metallo-drugs with novel mechanism of action [2]. Metal containing compounds may offer certain advantages over pure organic compound in drug therapy, i.e. the metal complexes may acts as a pro-drug [3], but solubility of these compounds was the main drawback for their higher efficacy and in clinical trials. Introduction of polar groups in organic moiety increase the hydrophilic nature of compounds has been recently investigated [4]. It was recently observed that fluorine containing organo-antimony compounds appeared to be a possible way to solve the water solubility problem and could also enhance the bio-medicinal efficacy of the compounds [5] and also offers a potentially rich field for the development of new medicinal agents with novel mechanisms of action. Bismuth based compounds have attracted remarkable attention and interest owing to their biological and medicinal utility [6-8].They have been used from more than two centuries in the treatment of gastrointestinal disorders such as dyspepsia, diarrhea and peptic ulcer[9-12]. Bismuth salts such as colloidal bismuth sub-citrate (CBS), bismuth sub-salicylate (BSS), and ranitidine bismuth citrate (RBC) are common agents used for *Helicobacter pylori* eradication therapy [13-15] and therefore promoted these compounds as antimicrobials. In search of antitumor studies, a variety of organobismuth compounds have been synthesized and tested *in-vitro* along with their antimicrobial activity [16-20]. The present manuscript deals the synthesis, structural and biomedicinal characterization along with gastroprotective studies of some novel fluorine based organic derivatives of bismuth. These compounds were synthesized by the method reported earlier and characterized with the help of M.P., elemental and I.R., NMR spectral analysis along with their antimicrobial studies, against different pathogenic bacterial and fungal strains and *in-vitro* antitumor activity against human breast (MCF-7) and mammary cancer (EVSA-7) cell line and found that compounds have potentiality as antitumor and antimicrobial agents. These compounds were also tested for gastroprotective (Anti-ulcer) activity in rats using standard methods.

Materials and Methods

The fluorine based diorganobismuth compounds *viz*; bis(pentafluorophenyl) bismuth (III) chloride was synthesized by the methods reported earlier [21] using metathetical reactions. The ligands were recrystallised before use. The reactions were performed under inert/nitrogen atmosphere. Preparation of representative organobismuth compounds are discussed below:

Reaction of $(C_6F_5)_2BiCl$ with $(OOC.C_6H_4.NO_2)$

Under nitrogen atmosphere, solution of bis(pentafluorophenyl)bismuth (III) chloride (1mmol) in benzene and 2-nitrobenzoic acid (1mmol) in same solvent were stirred together in presence of triethylamine at room temperature for 4-5 hours. The off-white color $Et_3N.HCl$ was formed (M.P. =240°C), which was filtered off and the filtrate on evaporation in vacuum gives an off-white color crystalline solid which was further recrystallised in pet-ether.

Reaction of $(C_6F_5)_2BiCl$ with $(OOC.C_6H_4.NO_2)$

In an oxygen free atmosphere, solution of bis(pentafluorophenyl)bismuth (III) chloride (1mmol) in benzene and 4-nitrobenzoic acid (1mmol) in same solvent were stirred together in presence of triethylamine at room temperature for 4-5 hours. The off-white color $Et_3N.HCl$ was formed (M.P. =240°C), which was filtered off and the filtrate on evaporation in vacuum gives an off-white color crystalline solid which was further recrystallised in pet-ether.

Reaction of $(C_6F_5)_2BiCl$ with $(OOC.C_6H_4.Cl)$

In an oxygen free inert atmosphere, solution of bis(pentafluorophenyl)bismuth (III) chloride (1mmol) in benzene and 2-chlorobenzoic acid (1mmol) in same solvent

were stirred together in presence of triethylamine at room temperature for 4-5 hours. The off-white color $Et_3N.HCl$ was formed (M.P. =240°C), which was filtered off and the filtrate on evaporation in vacuum gives an off-white color crystalline solid which was further recrystallised in pet-ether.

Reaction of $(C_6F_5)_2BiCl$ with $(OOC.C_6H_4.Cl)$

Under nitrogen atmosphere, solution of bis(pentafluorophenyl)bismuth (III) chloride (1mmol) in benzene and 4-chlorobenzoic acid (1mmol) in same solvent were stirred together in presence of triethylamine at room temperature for 4-5 hours. The off-white color $Et_3N.HCl$ was formed (M.P. =240°C), which was filtered off and the filtrate on evaporation in vacuum gives an off-white color crystalline solid which was further recrystallised in pet-ether.

Reaction of $(C_6F_5)_2BiCl$ with$[(OOC.C_6H_3(OH)(OCH_3)]$

In an oxygen free nitrogen atmosphere, solution of bis(pentafluorophenyl)bismuth (III) chloride (1mmol) in benzene and 3-methxy4-hydroxybenzoic acid (1mmol) in same solvent were stirred together in presence of triethylamine at room temperature for 4-5 hours. The off-white color $Et_3N.HCl$ was formed (M.P. =240°C), which was filtered off and the filtrate on evaporation in vacuum gives an off-white color crystalline solid which was further recrystallised in pet-ether.

Reaction of $(C_6F_5)_2BiCl$ with $(OOC.C_6H_4.NH_2)$

In an oxygen free nitrogen atmosphere, solution of bis(pentafluorophenyl)bismuth (III) chloride (1mmol) in benzene and 2-aminobenzoic acid (1mmol) in same solvent were stirred together in presence of triethylamine at room temperature for 4-5 hours. The off-white color $Et_3N.HCl$ was formed (M.P. =240°C), which was filtered off and the filtrate on evaporation in vacuum gives an off-white color crystalline solid which was further recrystallised in pet-ether.

Reaction of $(C_6F_5)_2BiCl$ with $(OOC.C_6H_4.NH_2)$

In an oxygen free nitrogen atmosphere, solution of bis(pentafluorophenyl)bismuth (III) chloride (1mmol) in benzene and 4-aminobenzoic acid (1mmol) in same solvent were stirred together in presence of triethylamine at room temperature for 4-5 hours. The off-white color $Et_3N.HCl$ was formed (M.P. =240°C), which was filtered off and the filtrate on evaporation in vacuum gives an off-white color crystalline solid which was further recrystallised in pet-ether.

Reaction of $(C_6F_5)_2BiCl$ with $[(OOC.C_6H_4.N(CH_3)_2)]$

In an oxygen free nitrogen atmosphere, solution of bis(pentafluorophenyl)bismuth (III) chloride (1mmol) in benzene and 3-dimethylaminobenzoic acid (1mmol) in same solvent were stirred together in presence of triethylamine at room temperature for 4-5 hours. The off-white color $Et_3N.HCl$ was formed (M.P. =240°C), which was filtered off and the filtrate on evaporation in vacuum gives an off-white color crystalline solid which was further recrystallised in pet-ether.

Reaction of $(C_6F_5)_2BiCl$ with $[(OOC.C_6H_4.N(C_2H_5)_2)]$

In an oxygen free nitrogen atmosphere, solution of bis(pentafluorophenyl)bismuth (III) chloride (1mmol) in benzene and 4-diethylaminobenzoic acid (1mmol) in same solvent were stirred together in presence of triethylamine at room temperature for 4-5 hours. The off-white color $Et_3N.HCl$ was formed (M.P. =240°C), which was filtered off and the filtrate on evaporation in vacuum gives an off-white color crystalline solid which was further recrystallised in pet-ether.

Antibacterial Activity:

The antibacterial activity of synthesized compound was carried out by disc diffusion method [22] 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.

Antifungal Activity:

The antifungal activity of the compound was tested by agar plate diffusion method [23], using ampicilin as standard. Four concentrations of the test compounds viz. 50 and 100 μg/ml were prepared and tested against two pathogenic fungal strains, *Aspergillus flavus* and *Aspergillus niger*. The 1 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 incubated 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 [24]. 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 color 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 ml) was added to each well of 96 well culture plate containing 100 ml 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 then 50 ml of DMSO was 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 fine out the optical density and cell count value.

Gastroprotective (Anti-ulcer) Activity:

The gastroprotective activity test of organobismuth compounds was performed in rats using standard methods [25]. In experiment, the rats were divided into four groups (each group contains 6 rats). Group 1 was control group which received suspension of 1% carboxymethyl cellulose in distilled water (10ml/kg). Group 2 and 3 received samples dose of 25 and 50 mg/kg body weight. Group 4 received ranitidine salt in the dose of 50mg/kg body weight. These all were administered orally twice daily at 10.00 and 16.00 hrs respectively for five days for acute ulcer protective studies.

- **Aspirin (ASP) Induced Ulcers*:*** Aspirin in dose of 200mg/ kg (20mg/ml) was administered to the animals on the day of the experiment and ulcers were scored after four hrs. The animals were sacrificed and the stomach was then excised and cut along the greater curvature, washed carefully with 5 ml of 0.9% NACL and ulcers were scored by a person unaware by the experimental protocol in the glandular portion of the stomach. Ulcer index was calculated by adding the total number of ulcers/ stomach & total severity of ulcers /stomach. The pooled group ulcer score was then calculated by reported method.
- **Ethanol (EtOH) induced Ulcers*:*** The gastric ulcers were induced in rats by administering ethanol (1ml/200gm/kg for 1hrs) and the animals were sacrificed by cervical dislocation & the stomach was incised along the greater curvature and examined for ulcers. The ulcer index was scored, based upon the product of length and width of the ulcers present in the glandular portion of the stomach (mm^2/rats).

Results and Discussion

The synthesis of bis(pentafluorophenyl)bismuth (III) carboxylates was performed in laboratory with the help of following reactions.

$$R_3Bi + BiCl_3 \xrightarrow{\text{Neat}} R_2BiCl$$

$$R_2BiCl + HL \xrightarrow{Et_3N} R_2BiL + Et_3N.HCl$$

Here:

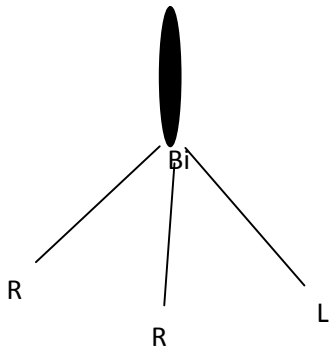
R = $[C_6F_5]$; HL = [Respective carboxylic acids]

All the newly synthesized bis(pentafluorophenyl)bismuth (III) carboxylates were crystalline solids, air stable and soluble in common organic solvents. The

compounds were further characterized by their melting points and analytical techniques such as elemental analysis, infrared and NMR spectroscopy to ascertain their structures and explore their biological properties. The new compounds have sharp melting points and posses pyramidal structure as per results obtained by further analysis.

IR and NMR Spectral Analysis:

The IR spectra of new bis(pentafluorophenyl)bismuth (III) carboxylates were recorded in Perkin–Elmer spectrophotometer in 4000-200 cm^{-1} range. The IR spectra of these compounds show absorption bands due to pentafluorophenyl groups. The absorption frequencies have been fully assigned. The Bi-C vibration in case of pentafluorophenyl derivatives corresponding to the 'y' mode appears in the range of 448-460 cm^{-1}. The IR data suggested a monodentate coordination mode of the carboxylate ligands. The ^{1}HNMR spectra of the representative bis (pentafluorophenyl) bismuth (III) carboxylate showed a multiplet in the range δ 7.82 ppm to δ 8.12 ppm which could be assigned to aromatic protons. The ^{19}FNMR spectra of the compound was carried out at room temperature and the compounds showed peaks appearing in the approximate range consistent with the presence of fluorophenyl groups. Thus on the basis of above discussions the newly synthesized bis(pentafluorophenyl)bismuth (III) compounds assigned a pyramidal structure.



R = (C_6F_5)
L = Respective Carboxylate as Ligands

Suggested structure of bis(pentafluorophenyl)bismuth (III) carboxylate

Antibacterial activity:

All the newly synthesized fluorine based bismuth (III) compounds show higher to moderate activity against the bacterial strains. It was found that compounds having water and lipid solubility are more effective. The compounds generally form complexes with metaloenzymes, particularly those which responsible in basic physiology such as *cytochrome oxidase*. These compounds may react with peptidoglycan layer of bacterial cell wall and damage it by penetrating in such a manner that the pentafluorophenyl ring gets entered inside the cell by puncturing it followed by death of bacterial cell. Sometimes these compounds in low concentration may cause bacteriostatic condition by slow down the growth of bacteria.

Antifungal Activity:

The antifungal activity of these compounds was found variable at 50μg/ml concentration but at higher concentration, all these compounds show high activity against fungal strains. Presence of fluorine, nitrogen, pentafluorophenyl ring along with bismuth in +3 oxidation state are considered for fungal activity. The role of different carboxylates as ligands was also commendable. These compounds generally damage the fungal strains by puncturing the cell wall similarly as in the case of bacteria. Water and lipid solubility also increases the activity.

***In-vitro* Antitumor Activity:**

The compounds show moderate to high activity against tumor cell lines. It was found that these compounds are in +3 oxidation state and the slight variation in their activity is due to presence of different carboxylate group as ligand. The compounds generally interact with the receptor site of multienzyme complex responsible for the cytostatic and cytotoxic conditions. It was reported that compounds in +3 oxidation state can easily bind with the receptor site. It may be noted that the organobismuth compound generally binds with nitrogen 7 position of purine bases in DNA molecule and form complexes with DNA strands affecting replication and transcription of DNA molecule and stop the cell division along with protein synthesis.

Gastroprotective Activity:

The compounds exhibit higher activity than the standard ranitidine when the tests were carried out with aspirin (ASP) induced and moderate activity was seen when the tests were done with ethanol (EtOH) induced. It was known that aspirin caused mucosal damage by interrupting the synthesis of prostaglandin and increasing acid secretion and back diffusion of H+ ions, which results in overproduction of leucotrienes and other products of 5-lipoxygenase pathway. Hence the protective action of these compounds against aspirin-induced gastric ulcer could possibly be due to its inhibitory effect on 5-lipoxygenase enzyme pathway. In case of ethanol induced ulcer which is predominantly occurs at glandular part of stomach was reported to stimulate the formation of leucotrienes C-4, mast cell secretary products and reactive oxygen species, which results in the damage of gastric mucosa of rat. The organobismuth compounds possibly play an important role in inhibition of these pathways and shows better activity.

Table-1 *Physicochemical Analysis of bis(pentafluorophenyl)bismuth (III) carboxylate*

S.N.	Compounds	Formula	Formula Weight	Yield %	M.P °C	Solvent	IR (cm^{-1})	
							ν_{asym}(CO)	ν_{sym}(CO)
1	$(C_6F_5)_2Bi(OOCC_6H_4NO_2)$	$C_{19}H_4F_{10}NO_4Bi$	709	68	58	Pet-Ether	1724vs	1326ms
2	$(C_6F_5)_2Bi(OOCC_6H_4NO_2)$	$C_{19}H_4F_{10}NO_4Bi$	709	66	59	Pet-Ether	1730vs	1334ms
3	$(C_6F_5)_2Bi(OOCC_6H_4Cl)$	$C_{19}H_4F_{10}O_2ClBi$	698.5	70	63	Pet-Ether	1732ms	1330ms
4	$(C_6F_5)_2Bi(OOCC_6H_4Cl)$	$C_{19}H_4F_{10}O_2ClBi$	698.5	72	61	Pet-Ether	1709 vs	1306ms
5	$[(C_6F_5)_2Bi(OOCC_6H_3(OH)OCH_3]$	$C_{20}H_7F_{10}O_4Bi$	710	66	62	Pet-Ether	1758vs	1356ms
6	$(C_6F_5)_2Bi(OOCC_6H_4NH_2)$	$C_{19}H_6F_{10}NO_2Bi$	679	65	66	Pet-Ether	1726ms	1325ms
7	$(C_6F_5)_2Bi(OOCC_6H_4NH_2)$	$C_{19}H_6F_{10}NO_2Bi$	679	65	67	Pet-Ether	1729vs	1327ms
8	$(C_6F_5)_2Bi(OOCC_6H_4N(CH_3)_2)$	$C_{21}H_{10}F_{10}NO_2Bi$	707	62	60	Pet-Ether	1752vs	1350ms
9	$(C_6F_5)_2Bi(OOCC_6H_4N(C_2H_5)_2)$	$C_{23}H_{14}F_{10}NO_2Bi$	735	60	57	Pet-Ether	1727ms	1325ms

Table-2 *Antibacterial Activity of bis(pentafluorophenyl)bismuth (III) carboxylate*

S. N.	Compounds	Control	Pseudomonas aeruginosa	Staphylococcus aureus	Klebsiela pneumoniae
1	$(C_6F_5)_2Bi(OOCC_6H_4NO_2)$	–	+++	++	++
2	$(C_6F_5)_2Bi(OOCC_6H_4NO_2)$	–	++	+	++
3	$(C_6F_5)_2Bi(OOCC_6H_4Cl)$	–	+++	++	++
4	$(C_6F_5)_2Bi(OOCC_6H_4Cl)$	–	++	++	++
5	$[(C_6F_5)_2Bi(OOCC_6H_3(OH)OCH_3]$	–	++	++	+++
6	$(C_6F_5)_2Bi(OOCC_6H_4NH_2)$	–	+++	+++	++
7	$(C_6F_5)_2Bi(OOCC_6H_4NH_2)$	–	+++	++	++
8	$(C_6F_5)_2Bi(OOCC_6H_4N(CH_3)_2)$	–	++	+	++
9	$(C_6F_5)_2Bi(OOCC_6H_4N(C_2H_5)_2)$	–	+++	++	++

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

Table-3 *Antifungal Activity of bis(pentafluorophenyl)bismuth (III) carboxylate at 50µg/ml conc.*

S. N.	Compounds	Aspergillus flavus Col. Dia. (mm)	% Inhibition	Aspergillus niger Col. Dia. (mm)	% Inhibition
1	$(C_6F_5)_2Bi(OOCC_6H_4NO_2)$	0.7	76.6	0.6	70.0
2	$(C_6F_5)_2Bi(OOCC_6H_4NO_2)$	0.7	76.6	0.5	75.0
3	$(C_6F_5)_2Bi(OOCC_6H_4Cl)$	0.5	83.3	0.4	80.0
4	$(C_6F_5)_2Bi(OOCC_6H_4Cl)$	0.2	93.3	0.7	65.0
5	$[(C_6F_5)_2Bi(OOCC_6H_3(OH)OCH_3]$	0.2	93.3	0.7	65.0
6	$(C_6F_5)_2Bi(OOCC_6H_4NH_2)$	0.4	86.7	0.6	70.0
7	$(C_6F_5)_2Bi(OOCC_6H_4NH_2)$	0.7	76.6	0.6	70.0
8	$(C_6F_5)_2Bi(OOCC_6H_4N(CH_3)_2)$	0.2	93.3	0.7	65.0
9	$(C_6F_5)_2Bi(OOCC_6H_4N(C_2H_5)_2)$	0.2	93.3	0.7	65.0
10	Control	3.0	-	2.0	-

Table-4 *Antifungal Activity of bis(pentafluorophenyl)bismuth (III) carboxylate at 100µg/ml conc.*

S. N.	Compounds	*Aspergillus flavus* Col. Dia. (mm)	% Inhibition	*Aspergillus niger* Col. Dia. (mm)	% Inhibition
1	$(C_6F_5)_2Bi(OOCC_6H_4NO_2)$	0.1	96.7	0.1	95.0
2	$(C_6F_5)_2Bi(OOCC_6H_4NO_2)$	0.4	86.7	0.2	90.0
3	$(C_6F_5)_2Bi(OOCC_6H_4Cl)$	0.2	93.3	0.2	90.0
4	$(C_6F_5)_2Bi(OOCC_6H_4Cl)$	0.1	96.7	0.4	80.0
5	$[(C_6F_5)_2Bi(OOCC_6H_3(OH)OCH_3]$	0.2	93.3	0.3	75.0
6	$(C_6F_5)_2Bi(OOCC_6H_4NH_2)$	0.1	96.7	0.3	75.0
7	$(C_6F_5)_2Bi(OOCC_6H_4NH_2)$	0.1	96.7	0.1	95.0
8	$(C_6F_5)_2Bi(OOCC_6H_4N(CH_3)_2)$	0.2	93.3	0.3	85.0
9	$(C_6F_5)_2Bi(OOCC_6H_4N(C_2H_5)_2)$	0.1	96.7	0.3	75.0
10	Control	3.0	--	2.0	--

Table-5: *Antitumor activity of bis(pentafluorophenyl)bismuth (III) carboxylate*

S. No.	Compounds	MCF-7 Cell No. x 10^4	EVSA-7 Cell No. x 10^4	Activity
1	$(C_6F_5)_2Bi(OOCC_6H_4NO_2)$	8.79 ± 0.52	8.42 ± 0.46	Positive
2	$(C_6F_5)_2Bi(OOCC_6H_4NO_2)$	9.19±0.92	9.29±0.88	Positive
3	$(C_6F_5)_2Bi(OOCC_6H_4Cl)$	8.95±0.67	8.55±0.62	Positive
4	$(C_6F_5)_2Bi(OOCC_6H_4Cl)$	12.31±1.02	12.39±1.03	Negative
5	$[(C_6F_5)_2Bi(OOCC_6H_3(OH)OCH_3]$	8.79 ± 0.52	8.42 ± 0.46	Positive
6	$(C_6F_5)_2Bi(OOCC_6H_4NH_2)$	9.29±0.88	9.89±0.92	Positive
7	$(C_6F_5)_2Bi(OOCC_6H_4NH_2)$	8.95±0.67	8.55±0.62	Positive
8	$(C_6F_5)_2Bi(OOCC_6H_4N(CH_3)_2)$	8.79 ± 0.52	8.42 ± 0.46	Positive
9	$(C_6F_5)_2Bi(OOCC_6H_4N(C_2H_5)_2)$	9.19±0.92	9.29±0.88	Positive
10	Negative control	10.21±1.01	10.22±1.01	–
11	Positive control	40.26±3.23	41.23±3.28	–

*Negative Control- Culture Medium only, **Positive Control – 17 β estradiol

Table-6 *Antiulcer Activity of bis(pentafluorophenyl)bismuth (III) carboxylate*

S.N.	Compounds	Aspirin Induced		Ethanol Induced	
		Ulcer Index (mm^2/rat)	Protective Ratio (%)	Ulcer Index (mm^2/rat)	Protective Ratio (%)
1	$(C_6F_5)_2Bi(OOCC_6H_4NO_2)$	7.1±0.54	61.21	19.6±5.3	33.72
2	$(C_6F_5)_2Bi(OOCC_6H_4NO_2)$	7.2±0.54	61.68	19.6±5.3	33.72
3	$(C_6F_5)_2Bi(OOCC_6H_4Cl)$	7.1±0.54	61.21	19.8±5.4	31.24
4	$(C_6F_5)_2Bi(OOCC_6H_4Cl)$	7.3±0.58	61.72	19.8±5.4	31.24
5	$[(C_6F_5)_2Bi(OOCC_6H_3(OH)OCH_3]$	6.2±0.28	62.16	14.4±2.2	34.70
6	$(C_6F_5)_2Bi(OOCC_6H_4NH_2)$	6.4±0.28	62.18	14.6±2.4	34.71
7	$(C_6F_5)_2Bi(OOCC_6H_4NH_2)$	6.2±0.28	62.16	19.8±5.4	31.24
8	$(C_6F_5)_2Bi(OOCC_6H_4N(CH_3)_2)$	7.3±0.58	61.72	19.8±5.4	31.24
9	$(C_6F_5)_2Bi(OOCC_6H_4N(C_2H_5)_2)$	6.2±0.28	62.16	14.4±2.2	34.70
10	Ranitidine	7.6±0.53	58.46	10.3±3.3	57.43
11	Aspirin	18.3±1.6	-	-	-
12	Ethanol	-		24.2±6.5	-

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