ISSN (Print 0974-2115) (Online 2349-8552)
www.jchps.com Journal of Chemical and Pharmaceutical Sciences

Evaluation of Anti-Inflammatory Activity of Substituted Benzofuran Derivatives

[1]Channamma G M*, [2]Basawaraj R, [1]Panchal C.V, [1]Patil S.S, [1]Poul B.N
[1]Department of Pharmaceutical Quality Assurance, Maharashtra College of Pharmacy, Nilanga, Maharashtra -413521
[2]Department of Pharmaceutical Chemistry, HKES's Matoshree Taradevi Rampure Institute of Pharmaceutical Sciences, Gulbarga, Karnataka -585105
***Corresponding Author: E-Mail: channagmaj@gmail.com, c.majage@yahoo.in, Phone: 8073825409**

ABSTRACT

Benzofuran and its derivatives constitute active group of compounds bearing comprehensive biotic and pharmacological activities.

Reaction of 5-Bromosalicyldehyde with 2-Bromo-1-(Phenyl) ethanones yields 5-Bromobenzofuran-2-yl-phenyl methanone (1a-e). Condensation of compounds (1a-e) with Aniline, Hydroxylamine hydrochloride and Thiosemicarbazide afforded [(5-Bromo benzofuran-2-yl)[phenyl]methylene]aniline(2a-e),(5-Bromobenzofuran-2-yl) (phenyl) methanone oxime (3a-e) and [(5-Bromobenzofuran-2-yl)(phenyl)methylene]hydrazine carbothioamide (4a-e) respectively.

KEY WORDS: Benzofuran, 5-Bromosalicyldehyde, Hydroxylamine hydrochloride, Thiosemicarbazide, Anti-inflammatory activity.

1. INTRODUCTION

Benzofuran is an important heterocyclic compound with varied biological activities. Large number of Benzofuran and its derivatives were acknowledged to present in natural products and reported to possess anticonvulsant, sedative, hypnotic, antibacterial, antifungal, CNS stimulant and anti-inflammatory activities (Simpson, 1985; Basawaraj, 2008; Aruna Kumar, 2007; Balzarini and Guigane, 2002; Santana, 1999).

By seeing impressive biological profile of Benzofuran and also with respect to our work in synthesis and evaluation of biologically active substituted Benzofuran derivatives from (5-Bromobenzofuran-2-yl)(phenyl)methanone(1a-e) as potent anti-inflammatory activity.

The objective of this work is to certain substituted Benzofuran derivatives of more potent and less toxic newer drugs of biological interest.

2. MATERIAL AND METHODS

Melting points are in degree Celsius, were determined in open capillary tubes in paraffin oil bath and melting point instrument are uncorrected. Purity of the compounds was established by TLC analysis on pre-coated Silica gel plates. The spots visualization on TLC plates was achieved by UV light. The completion of reaction and purity was monitored by TLC. Infrared spectrum were recorded on FTIR-8400S (SHIMADZU) spectrophotometer, Perkin-Elmer 1000 spectrometer in KBr. The ^{1}H-NMR spectra were recorded on Bruker Avance II of 400 MHz spectrophotometer. Mass spectrum were recorded on LCMS 2010A data report Shimadzu Japan.

Synthesis of 2-Bromo-1-phenylethanone: A solution of Aceto phenone (0.02 mole) in Acetic acid (100ml) to this solution added Bromine (0.018 mole) in Acetic acid slowly with constant stirring. Mixture was kept at room temperature for 5 hrs, after completion of reaction then it was poured in to ice cold water. The solid separated was collected and crystallized out from Methanol to get a purified compound of 2-Bromo-1-phenylethanone (Yield 68%), m.p 50-52^{0}C.

Synthesis of (5-Bromobenzofuran-2-yl)(phenyl)methanone (1a-e): An equimolar quantity of 5-Bromosalicyladehyde(0.01mole), 2-Bromo-1-(phenyl)ethanone(0.02mole) and add Potassium carbonate (0.03mole) in Dimethyl formamide was heated at 80^{0}C for 5 hrs. Reaction compound were cooled to room temperature and then poured into ice cooled water. The solid product was separated by filtration and crystallized from Ethanol. Physical characterization details of compounds were shown in table.1.

Synthesis of [(5-Bromobenzofuran-2-yl)(phenyl)methylene]aniline (2a-e): The mixture of (1a-e) (0.003 mole) and Aniline (4ml) in absolute Ethanol (30 ml). The reaction was refluxed for 4 hrs, thus solid obtained filtered, washed by the water and recrystallized from solvent Ethanol. The physical data of compounds were summarized in table.1.

Synthesis of [(5-Bromobenzofuran-2-yl)(phenyl)methanone]oxime (3a-e): The compounds (1a-e) (0.003 mole) and Hydroxylamine hydrochloride (0.00 3 mole) in solvent Pyridine (4 ml) were placed in a round bottomed flask fitted with reflux condenser. Reaction mixture, refluxed 6 hrs. After cooling reaction content, poured to ice cold water and thus solid separated were filtered and washed several times with water and crystallized using Ethanol. The physical characterization data of compounds were shown in table.1.

Synthesis of [(5-Bromobenzofuran-2-yl)(phenyl)methylene]hydrazinecarbothioamide (4a-e): A mixture of (1a-e) (0.003 mole) and Thiosemicarbazide (0.003 mole) in absolute Ethanol (30 ml) was refluxed for 4 hrs. The course of reaction was monitored by TLC, solvent removed by reduced pressure, the residue was treated with water and solid thus separated was collected and recrystallized from Ethanol. Physical characteristics data of compounds were shown in table.1.

SCHEME

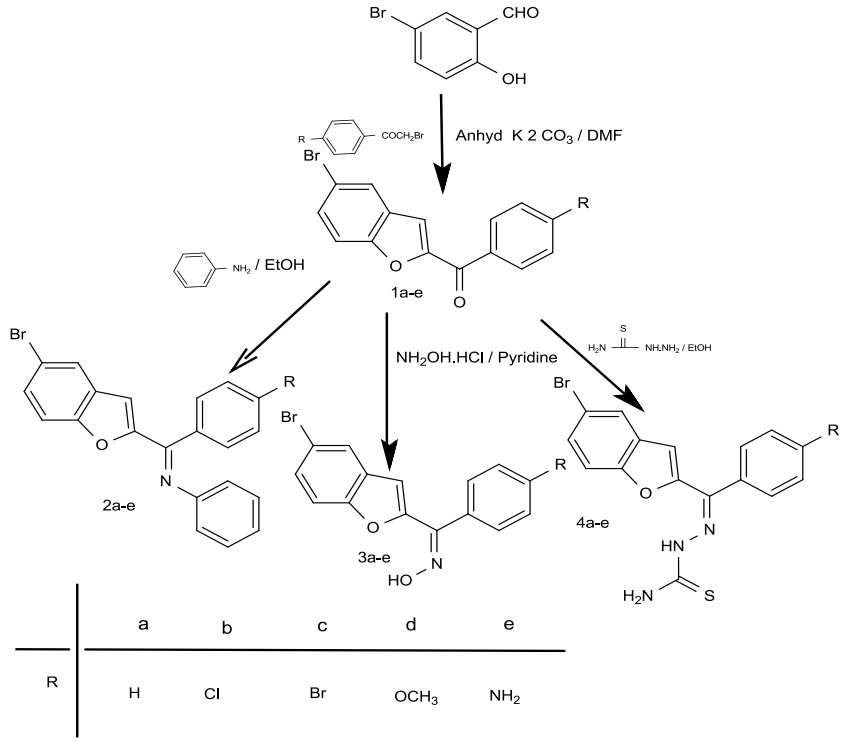

Table.1. Physical characterisation data of compounds (1a-e), (2a-e), (3a-e) and (4a-e)

Compound code	R	Molecular Formula	Molecular weight	m.p (^{0}C)	% Yield
1a	H	$C_{15}H_9BrO_2$	301.13	105-107	52
1b	Cl (p)	$C_{15}H_8BrClO_2$	335.57	188-190	59
1c	Br (p)	$C_{15}H_8Br_2O_2$	380.03	122-124	61
1d	OCH_3(p)	$C_{16}H_{11}BrO_3$	331.16	187-189	67
1e	NH_2(p)	$C_{15}H_{10}BrNO_2$	316.14	183-185	60
2a	H	$C_{21}H_{14}BrNO$	376.24	154-156	64
2b	Cl (p)	$C_{21}H_{13}BrClNO$	410.69	189-191	62
2c	Br (p)	$C_{21}H_{13}Br_2NO$	455.14	182-184	63
2d	OCH_3(p)	$C_{22}H_{16}BrNO_2$	406.27	168-170	51
2e	NH_2(p)	$C_{21}H_{15}BrN_2O$	391.26	233-235	60
3a	H	$C_{15}H_{10}BrNO_2$	316.14	145-147	58
3b	Cl (p)	$C_{15}H_9BrClNO_2$	350.59	177-179	56
3c	Br (p)	$C_{15}H_9Br_2NO_2$	395.04	187-189	65
3d	OCH_3(p)	$C_{16}H_{12}BrNO_3$	346.17	128-130	54
3e	NH_2(p)	$C_{15}H_{11}BrN_2O_2$	331.16	166-168	61
4a	H	$C_{16}H_{12}BrN_3OS$	374.25	118-120	52
4b	Cl (p)	$C_{16}H_{11}Br\ ClN_3OS$	408.70	180-182	66
4c	Br (p)	$C_{16}H_{11}Br_2N_3OS$	453.15	190-192	63
4d	OCH_3(p)	$C_{17}H_{14}BrN_3O_2S$	404.28	138-140	59
4e	NH_2(p)	$C_{16}H_{13}BrN_4OS$	389.26	196-198	52

Spectral Data:

Compound	IR (cm^{-1})	^{1}H-NMR (ppm)δ	Mass (m/z)
2d	3118 CH strt, 2921 CH str of OCH_3, 1600 C=N str, 1550, 1448 C=Cstrt, 761 C-Br str of Ar	3.89 s, 3H of OCH_3	406 (M^{+1})
2e	3365 NH str, 1585 C=N str, 1409,1330 C=C str, 736 C-Br str	5.25 s 2H of NH_2. 7.26 - 8.22 m, Ar-H	391(M^{+1})
3a	3465 OH strt, 1560 C=N strt, 1301 C=C str, 757 C-Br strt	9.49 s, 1H OH. 6.48-7.42 m, Ar-H.	315(M^{+1})
3d	3265 OH str, 2921 CH str OCH_3 , 1606 C=N str, 1024 C-O str, 676 C-Br str	9.31 s, 1H, OH. 7.00-7.40 m, Ar-H. 3.59, s, 3H OCH_3	346(M^{+1})
4d	3384,3251 NH str, 3132 CH str Ar, 2952 CH str OCH_3, 1637 C=N str, 1531,1452 C=Cstr, 761C-Br str	3.89s, 3H OCH_3. 9.20 s, 1H, NH. 7.34-8.45 m, Ar-H. 5.27 s, 2H NH_2	404(M^{+1})
4e	3363 NH str , 1033 C-N str, 1595 C=N str, at 732 C-Br str.	5.28 s, 2H, Ph-NH_2. 8.12 s, 2H C-NH_2 7.26-7.99 m, Ar-H. 9.20 s,1H N-NH	389(M^{+1})

Anti-Inflammatory Activity: The (5-Bromobenzofuran-2-yl) (phenyl)methanone derivatives were screened for their anti-inflammatory activity using Carrageenan induced rat paw oedema model (Ghosh, 2005; Cotran, 2001). Diclofenac sodium 4.5mg/kg b.w. suspension in 1% gum acacia was used as standard drug (Kulkarni, 1993).

3. RESULT AND DISCUSSION

In the present work the number of Benzofuran derivatives was synthesized. The synthesized compounds characterized by spectral and analytical studies. Among the selected compounds of (5-Bromobenzofuran-2-yl)(phenyl)methanone derivatives, (2a-c), (3a-c) and (4a-c) screened for anti-inflammatory activity against standard drug Diclofenac sodium. The compounds (2b), (2c) and (4b) showed moderate activity.

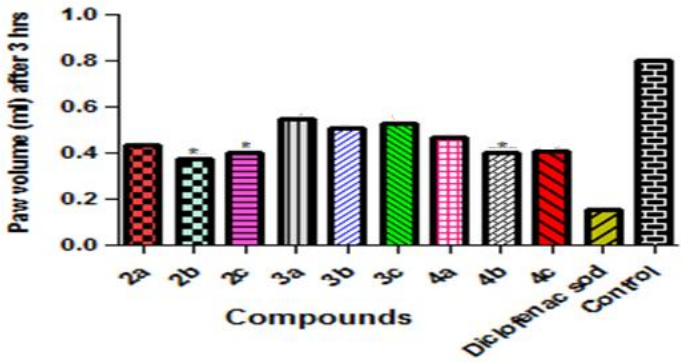

Figure.1. Graphical representation of anti-inflammatory activity of selected compounds

Table.2. Anti-inflammatory activity data of selected compounds

Compound Code	Dose mg/kg	Mean difference in paw volume (± S.E) at 3hrs(ml)	% inhibition of inflammation
2a	50	0.44(± 0.005)	45.00
2b	50	0.38(± 0.005)*	52.00
2c	50	0.40(± 0.005)*	50.00
3a	50	0.55(± 0.002)	31.25
3b	50	0.51(± 0.005)	36.25
3c	50	0.53(± 0.004)	33.75
4a	50	0.47(± 0.002)	41.2
4b	50	0.40(± 0.005)*	50.00
4c	50	0.41(± 0.006)	48.75
Diclofenac sodium	4.5	0.16(± 0.001)	82.25
Control	-	0.80(±0.009)	-

Significance at *P<0.05(n=6)

Statistical Analysis: The results obtained from the study were given as mean ± standard error mean (SEM). The results were analysed with variance (ANOVA), followed by Dunnet's test, were test compound groups was compared with control group. Values of 'p' statistically significant.

4. CONCLUSION

The main aim and objective of the work was to synthesize substituted Benzofuran derivatives of pharmacological interest. Some of the selected compounds showed moderate anti-inflammatory activity, when compared with standard drug. Thus an attempt has been undertaken to study some selected compounds at different concentrations.

5. ACKNOWLEDGEMENT

The authors would like to acknowledge Management of Maharashtra college of Pharmacy, Nilanga for the support and encouragement. Authors are grateful to Dr. S. S. Patil and C.V. Panchal for valuable suggestions during preparation of manuscript. The authors also would like to acknowledge Dr. B.V. Raga for helpful discussion in laboratory work.

REFERENCES

Aruna Kumar D B, Prakash G K, Kumaraswamy M N, Nandeshwarappa B P, Sherigara B S and Mahadevan K M, Synthesis and Antimicrobial Investigation of Some Novel Phenyl Pyrazole, Azetidinone and Diazenyl Ethanone Derivatives of Benzofurans, Indian J, Chem., 46B, 2007, 336-343.

Balzarini J and Guigane Mc, Biocyclic pyrimidine nucleoside analogues as highly selective & potent inhibitors of varicella-zoster virus replication, J. Antimicrob Chemother, 50, 2002, 5-9.

Basawaraj R, Goled S, Kalaskar G and Sangapure S, Reaction products of 2-substituted-4-chlorobenzofuro[3,2-d]pyrimidine & their anti-microbial activities, Indian J. of Heterocyclic Chem., 18, 2008, 1-4.

Cotran R.S, Kurma V, Collins T and Robbins, Pathological basis of disease, VIth Edn., W.B. Saunder's Company New York, 2001.

Ghosh M.N, Fundamentals of experimental pharmacology, 3rd Edition, 2005, 192-193.

Kulkarni S.K, Hand Book of Experimental Pharmacology, Vallabh Prakashan, Delhi, India, 1993, 50.

Santana L, Teijeira M, Uriarte E & Cano T, AMI theoretical study, Synthesis & biological evaluation of some benzofuran analogues of anti-inflammatory aryl alkanoic acids, Eur J Pharm Sci, 7 (2), 1999, 161-166.

Simpson T.J, Aromatic Compounds, in The Chemistry of Natural Products, edited by Thomson R H, Blackie London, 1985.