ANTI HISATMINIC ACTIVITY OF NEW ISATIN DERIVATIVES

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ABSTRACT

Forty two New 2-{(benzalamino-4-hydroxybenzyl) (1,3,4)-oxadiazino[6,5-b]} Indole derivatives (V) have been synthesized by condensing 2-Amino-4-[(1,3,4)oxadiazino[6,5-b]indole-3-yl]-phenol (IV) with various aromatic aldehydes. The intermediates, on the other hand, have been synthesized by the cyclization of 3-Amino-4-hydroxy-benzoic acid (2-oxo-1,2-dihydro-indol-3-ylidene)-hydrazide (III) in presence of Concentrated H_2SO_4. The title compounds have been purified and characterized by their analytical and spectral data. They have screened for their antihistaminic activity and all the forty two compounds showed very good anti histaminic activity. Compounds V_6 and V_{41} showed potent antihistaminic activity with IC_{50} values 3.25×10^{-5} mol/lit and 4.10×10^{-5} mol/lit respectively.

KEY WORDS : (1,3,4)-oxadiazino-[6,5-b]indole, Isatin derivatives, Anti histaminic activity.

1.INTRODUCTION

It is known from the literature that indole derivatives exhibit varied biological and pharmacological properties (Sarangapani,2001; Pandeya,2003; Sarangapani,1998; Khan and Akhtar,2003; Singh,1983; Anku patel,2006; Bari,2008; Sarangapani and Reddy,1999) viz. antimicrobial, antiviral, anti neoplastic, analgesic, CNS activities. In view of theses observations the synthesis of New 2-{(benzalamino-4-hydroxybenzyl) (1,3,4)-oxadiazino[6,5-b]} Indole derivatives (V) has been carried out.

For this purpose the required indole-2,3-diones (I) were prepared and condensed with 3-amino-4-hydroxybenzoicacidhydrazide(II) in ethanol to get the respective 3-Amino-4-hydroxy-benzoic acid (2-oxo-1,2-dihydro-indol-3-ylidene)-hydrazide (III). These compounds were cyclized using concentrated sulfuric acid to get respective 2-Amino-4-[(1,3,4) oxadiazino [6,5-b]indole-3-yl]-phenol(IV).These compounds were refluxed with aromatic aldehyde,ethanol and few drops of acetic acid to get the title compounds. The compounds were characterized by their physical, analytical and spectral data (IR,PMR and MASS). The data on Antihistaminic activity is presented in Table I.

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2.METHODS

Experimental

Antihistaminic activity

The H_1 antihistaminic activity (Reuse,1948) of the test compounds was determined in *vitro* by the isolated guinea pig ileum method. Taking log doses of the test compounds and spasms were induced by a sub maximal concentration of histamine dihydrochloride. Diphenhydramine hydrochloride was used as reference standard (IC_{50} 5.02×10^{-7} mol/lit). The IC50 values of the test compounds were calculated graphically. Triplicate test were done at each concentration level of the compound. The results of antihistaminic activity of title compounds are presented in TableI.

3.RESULTS AND DISCUSSION

All the forty two compounds have been evaluated for their *in-vitro* H_1 antihistaminic activity using isolated guinea pig ileum method, by using diphenhydramine as standard drug. The results of antihistaminic activity are presented in Table I. The results revealed that all the forty two compounds showed antihistaminic activity. Among the forty two compounds, compounds V_6 ($R^1 = R^2 = H$, $R^3 = N(CH_3)_2$, $R^4 = H$) and V_{41} ($R^1 = CH_3$, $R^2 = H$, $R^3 = N(CH_3)_2$, $R^4 = H$) showed potent antihistaminic activity with IC_{50} values 3.25×10^{-5} mol/lit and 4.10×10^{-5} mol/lit respectively. However, it is interesting to note that a few of the compounds in this series V_{13}, V_{20}, V_{27}, V_{34}, with terminal N,N dimethylamino group showed good antihistaminic activity with IC_{50} values of 4.96×10^{-5}, 5.72×10^{-5}, 4.67×10^{-5}, 6.10×10^{-5} respectively. The rest of the

compounds showed poor anti histaminic activity as their IC_{50} values are considerably higher than the standard diphenhydramine.

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REFERENCES

Anku Patel, Sanjay bari, Gokul Talele, Jitendra Patel and Manda Sarangapani, Synthesis and Antimicrobial Activity of Some New Isatin Derivatives, Iranian Journal of Pharmaceutical research, 4, 2006, 249-254.

Bari S.B, Agrawal A.O and Patel U.K, Synthesis and Pharmacological Evalution of Some Novel Isatin derivatives for Antimicrobial Activity, Journal of Science, Islamic Republic of Iran, 19(3), 2008, 217-221.

Khan M.S.Y and Akhtar M, Synthesis of Some New 2,5-Disubstituted 1,3,4 –Oxadiazole Derivatives and Their Biological Activity, Indian journal of Chemistry, 42B, 2003, 903-904.

Pandeya S.N, Laximi V.S and Pandeya A, Biological Activity of Mannich Bases, Indian J. Pharma. Science, 65(3), 2003, 213-222.

Reuse J.J, British journal of pharmacology, 3, 1948, 174.

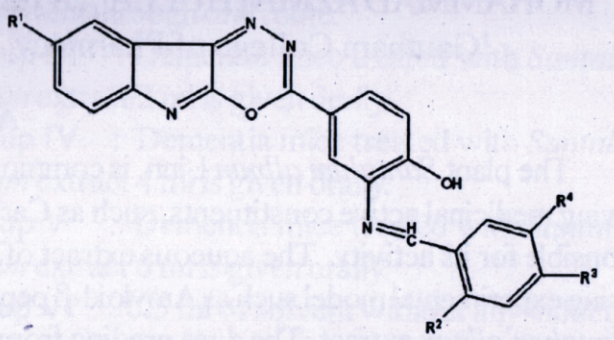
Sarangapani M, Jessy Jacob, Srinivas B and Raghunandan N, Synthesis and CNS Activity of New Indole Derivatives, Indian Drugs, 38(5), 2001, 264-268.

Sarangapani M, Narayana Reddy A, Jayamma Y, Reddy V.M, Synthesis and Pharmacological Activity of New Hydrazones, Indian Drugs, 35(6), 1998, 336-343.

Sarangapani M and Reddy V.M, Synthesis and screening of Isatin-3-[N^2-(alkoxyethyloxy) acetyl] hydrazones, Indian drugs, 36(6), 1999, 357-362.

Singh S.P, Shukla S.K and Awasthi L.P, Synthesis of Some 3-(4'-Nitrobenzoyl hydrazono)-2-Indolinone as Potential Anti-Viral Agents, Current Science, 52(16), 1983.

Table I: Data on Antihistaminic activity of New 2-{(benzalamino-4-hydroxybenzyl) (1,3,4)-oxadiazino[6,5-b] } Indole derivatives (V)



Compound	Substituents				IC_{50} Value (mol/lit)
	R^1	R^2	R^3	R^4	
Diphenhydramine HCl	--	--	--	--	5.02×10^{-7}
V(1)	H	H	H	H	2.50×10^{-4}
V(2)	H	H	Cl	H	3.22×10^{-4}
V(3)	H	OH	H	H	3.67×10^{-4}
V(4)	H	H	OCH_3	H	2.90×10^{-4}
V(5)	H	H	OCH_3	OCH_3	3.10×10^{-4}
V(6)	H	H	$N(CH_3)_2$	H	3.25×10^{-5}
V(7)	H	H	OH	OCH_3	3.56×10^{-4}
V(8)	Br	H	H	H	2.45×10^{-4}
V(9)	Br	H	Cl	H	3.67×10^{-4}
V(10)	Br	OH	H	H	2.75×10^{-4}
V(11)	Br	H	OCH_3	H	3.47×10^{-4}
V(12)	Br	H	OCH_3	OCH_3	3.21×10^{-4}
V(13)	Br	H	$N(CH_3)_2$	H	4.96×10^{-5}
V(14)	Br	H	OH	OCH_3	3.71×10^{-4}
V(15)	NO_2	H	H	H	3.57×10^{-4}
V(16)	NO_2	H	Cl	H	2.61×10^{-4}
V(17)	NO_2	OH	H	H	4.41×10^{-4}
V(18)	NO_2	H	OCH_3	H	3.67×10^{-4}
V(19)	NO_2	H	OCH_3	OCH_3	2.61×10^{-4}
V(20)	NO_2	H	$N(CH_3)_2$	H	5.72×10^{-5}
V(21)	NO_2	H	OH	OCH_3	4.41×10^{-4}
V(22)	F	H	H	H	3.51×10^{-4}
V(23)	F	H	Cl	H	5.60×10^{-4}
V(24)	F	OH	H	H	3.21×10^{-4}
V(25)	F	H	OCH_3	H	2.93×10^{-4}
V(26)	F	H	OCH_3	OCH_3	3.72×10^{-4}
V(27)	F	H	$N(CH_3)_2$	H	4.67×10^{-5}
V(28)	F	H	OH	OCH_3	4.30×10^{-4}
V(29)	Cl	H	H	H	2.90×10^{-4}
V(30)	Cl	H	Cl	H	3.60×10^{-4}
V(31)	Cl	OH	H	H	3.71×10^{-4}
V(32)	Cl	H	OCH_3	H	4.2×10^{-4}
V(33)	Cl	H	OCH_3	OCH_3	4.10×10^{-4}
V(34)	Cl	H	$N(CH_3)_2$	H	6.10×10^{-5}
V(35)	Cl	H	OH	OCH_3	4.40×10^{-4}
V(36)	CH_3	H	H	H	3.1×10^{-4}
V(37)	CH_3	H	Cl	H	3.60×10^{-4}
V(38)	CH_3	OH	H	H	4.15×10^{-4}
V(39)	CH_3	H	OCH_3	H	3.62×10^{-4}
V(40)	CH_3	H	OCH_3	OCH_3	2.31×10^{-4}
V(41)	CH_3	H	$N(CH_3)_2$	H	4.10×10^{-5}
V(42)	CH_3	H	OH	OCH_3	3.04×10^{-4}

Standard: Diphenhydramine HCl