Synthesis of *(E)-N′*-[1-(2,4-Dihydroxyphenyl)ethylidene]Substituted Hydrazides as Possible *α*-glucosidase and butyrylcholinesterase Inhibitors

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Summary: In the current research work, *(E)-N′*-[1-(2,4-dihydroxyphenyl)ethylidene]substituted hydrazides were synthesized in a couple of steps and their enzyme inhibition potential was analyzed. Firstly 2,4-hydroxyacetophenone (**1**) was reacted with hydrated hydrazine (**2**) under stirring to yield *(E)*-4-(1-hydrazonoethyl)benzene-1,3-diol (**3**) which was further reacted with different acid halides, (**4a-i**) to afford *(E)*-[1-(2,4-dihydroxyphenyl)ethylidene]substituted hydrazides (**5a-i**). These synthesized compounds were characterized by EI-MS, ^{1}H-NMR spectral techniques and were also evaluated against *α*-glucosidase and butyrylcholinesterase enzymes. The synthesized compounds were found to be acceptable inhibitors of *α*-glucosidase and decent inhibition against butyrylcholinesterase.

Keywords: 2,4-Dihydroxyacetophenone, Hydrated hydrazine, Acid halides, *α*-Glucosidase, Butyrylcholinesterase.

Introduction

Hydrazones and their derivatives comprise a resourceful class of compounds in organic chemistry. These compounds have fascinating biological properties, which include anti-inflammatory, anti-convulsant, analgesic, anti-tumor, anti-tuberculosis, anti-HIV and anti-microbial activity [1]. Hydrazones are essential compounds for drug design, as doable ligands for metal complexes, organocatalysis and moreover for the synthesis of heterocyclic compounds [2]. Azomethine are products by condensation of simple acid hydrazide with aceto group containing compound in the presence acetic acid catalyst in the appropriate solvent and suitable condition. Some of azomethine show a wide range of biological activities as anti-inflammatory, anti-bacterial, anti-fungal and anti-oxidant agents [3-6]. Some of the hydrazides are already prepared [7] and have been investigated for the treatmrnt of cancer [8].

α-Glucosidase inhibitors are used as oral anti-diabetic drugs for type-2 *Diabetes mellitus*. Postprandial hyperglycemia has a vital role in the development of type-2 diabetes and the associated complications [9]. These inhibitors retard the liberation of D-glucose of oligosaccharides and disaccharides from dietary complex carbohydrates and so delay glucose absorption, resulting in reduction of postprandial hyperglycemia [10]. Butyrylcholinesterase (BChE, EC 3.1.1.8) constitutes a family of enzymes which include serine hydrolases. The different specificities for substrates and inhibitors for these enzymes are due to the differences in amino acid residues of the active sites of BChE. The enzyme system is responsible for the termination of acetylcholine at cholinergic synapses. These are key components of cholinergic brain synapses and neuromuscular junctions. The major function of BChE is to catalyze the hydrolysis of the neurotransmitter acetylcholine and termination of the nerve impulse in cholinergic synapses [11, 12].

In continuation of our previous efforts [13-17] and in search of new therapeutic agents having less toxicity we report herein a facile and benign synthesis of different *N*-substituted hydrazides, derived from 1-(2,4-dihydroxyphenyl)-1-ethanonehydrazone, which might be utilized for the treatment of various inflammatory diseases.

Experimental

General

^{1}H-NMR spectra were recorded in CD_3OD on a Burker Aspect AM-300 MHz spectrometer. Chemical shifts (*δ)* are given in ppm. Mass spectra

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(EI-MS) were measured on Finnigan MAT-112 instrument. TLC was performed on pre-coated silica gel G-25-UV_{254} plates. Detection was carried out at 254 nm, and by ceric sulphate reagent. Purity was checked by TLC with different percentages of ethyl acetate and *n*-hexane as mobile phase.

Synthesis

(E)-4-(1-Hydrazonoethyl)benzene-1,3-diol (**3**)

2,4-Dihydroxyacetophenone (1.9 mmol, **1**) was solubilized in 20 mL methanol and was taken in a 100 mL round bottom flask. Equimolar quantity of hydrated hydrazine (1.9 mmol, 80 %, **2**) along with two drops of glacial CH_3COOH was added to the reaction mixture which was stirred for 3-4 hours till completion of reaction monitored by the TLC. The excess of solvent was removed by distillation followed by the addition of distilled water to afford precipitates which were filtered, washed with distilled water and dried to obtain pure *(E)*-4-(1-hydrazonoethyl)benzene-1,3-diol as light yellow amorphous solid (**3**) having 82 % yield.

(E)-N'-[1-(2,4-dihydroxyphenyl)ethylidene]substituted hydrazides (**5a-i**)

(E)-4-(1-hydrazonoethyl)benzene-1,3-diol (0.1mmol, **3**) was dissolved in 15 mL methanol was taken in a 50 mL round bottom flask. Two drops of CH_3COOH (glacial) and different acid halides (0.1mmol, **4a-i**) were added and the reaction mixture which was stirred for 3-4 hours till completion of reaction confirmed *via* TLC. The reaction mixture was quenched with cold distilled water to get pure precipitates of *(E)-N'*-[1-(2,4-dihydroxyphenyl)ethylidene]substituted hydrazides (**5a-i**).

Spectral Characterization

(E)-N'-[1-(2,4-Dihydroxyphenyl)ethylidene]acetohydrazide (**5a**)

Light yellow amorphous solid; Yield: 88 %; m.p.: 154-156 ^oC; Mol. F.: $C_{10}H_{12}N_2O_3$; Mol. mass: 208 $gmol^{-1}$; IR (KBr, υ_{max}/cm^{-1}): 3252 (O-H), 3040 (Ar C-H), 1665 (C=N), 1614 (Ar C=C); ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 7.95 (s, 1H, NH), 7.59 (d, J = 9.6 Hz, 1H, H-6), 6.80 (d, J = 9.5 Hz, 1H, H-5), 6.85 (s, 1H, H-3), 2.44 (s, 3H, CH_3-1''), 1.50 (s, 3H, CH_3-1'); EI-MS (*m/z*): 208 $[M]^+$, 193 $[C_9H_9N_2O_3]^+$, 165 $[C_8H_9N_2O_2]^+$, 150 $[C_8H_8NO_2]^+$, 137 $[C_8H_9O_2]^+$, 109 $[C_6H_5O_2]^+$, 99 $[C_4H_7N_2O]^+$, 43 $[C_2H_3O]^+$.

(E)-N'-[1-(2,4-Dihydroxyphenyl)ethylidene]-2-bromoacetohydrazide (**5b**)

Light yellow amorphous solid; Yield: 90 %; m.p.: 154-156 ^oC; Mol. F.: $C_{10}H_{11}BrN_2O_3$; Mol. mass: 286 $gmol^{-1}$; IR (KBr, υ_{max}/cm^{-1}): 32454(O-H), 3049 (Ar C-H), 1669 (C=N), 1622 (Ar C=C); ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 7.97 (s, 1H, NH), 7.56 (d, J = 9.6 Hz, 1H, H-6), 6.89 (d, J = 9.5 Hz, 1H, H-5), 6.81 (s, 1H, H-3), 4.31 (s, 2H, CH_2-1'), 2.42 (s, 3H, CH_3-1''); EI-MS (*m/z*): 286 $[M]^+$, 271 $[C_9H_8BrN_2O_3]^+$, 193 $[C_9H_9N_2O_3]^+$, 176 $[C_4H_6BrN_2O]^+$, 165 $[C_8H_9N_2O_2]^+$, 150 $[C_8H_8NO_2]^+$, 150 $[C_7H_4NO_3]^+$, 137 $[C_8H_9O_2]^+$, 120 $[C_2H_2BrO]^+$, 109 $[C_6H_5O_2]^+$.

(E)-N'-[1-(2,4-Dihydroxyphenyl]ethylidene)benzohydrazide (**5c**)

Off white amorphous solid; Yield: 82 %; m.p.: 233-235 ^oC; Mol. F.: $C_{15}H_{14}N_2O_3$; Mol. mass: 270 $gmol^{-1}$; IR (KBr, υ_{max}/cm^{-1}): 3255 (O-H), 3046 (Ar C-H), 1662 (C=N), 1611 (Ar C=C); ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 7.97 (s, 1H, NH), 7.56 (d, J = 9.5 Hz, 1H, H-6), 7.36 (d, J = 8.4 Hz, 2H, H-2' and H-6'), 7.26 (dt, J = 8.0 Hz, 1H, H-4'), 7.21-7.18 (m, 2H, H-3' and H-5'), 6.80 (d, J = 9.5 Hz, 1H, H-5), 6.82 (s, 1H, H-3), 2.49 (s, 3H, CH_3-1''); EI-MS (*m/z*): 270 $[M]^+$, 255 $[C_{14}H_{11}N_2O_3]^+$, 206 $[C_9H_8N_3O_3]^+$, 193 $[C_9H_9N_2O_3]^+$, 165 $[C_8H_9N_2O_2]^+$, 161 $[C_9H_9N_2O]^+$, 150 $[C_8H_8NO_2]^+$, 137 $[C_8H_9O_2]^+$, 109 $[C_6H_5O_2]^+$, 105 $[C_7H_5O]^+$.

(E)-N'-[1-(2,4-Dihydroxyphenyl)ethylidene]-2-chlorobenzohydrazide (**5d**)

Off-white amorphous solid; Yield: 88 %; m.p.: 160-162 ^oC; Mol. F.: $C_{15}H_{13}ClN_2O_3$; Mol. mass: 304 $gmol^{-1}$; IR (KBr, υ_{max}/cm^{-1}): 3240 (O-H), 3039 (Ar C-H), 1658 (C=N), 1621 (Ar C=C); ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 7.99 (s, 1H, NH), 7.72 (d, J = 8.4 Hz, 1H, H-6'), 7.61 (dd, J = 9.6 Hz, 1H, H-4'), 7.58 (d, J = 9.6 Hz, 1H, H-6), 7.50 (dt, J = 8.0 Hz, 1H, H-5'), 6.86 (d, J = 9.6 Hz, 1H, H-5), 6.83 (s, 1H, H-3), 2.45 (s, 3H, CH_3-1''); EI-MS (*m/z*): 304 $[M]^+$, 289 $[C_{14}H_{10}ClN_2O_3]^+$, 195 $[C_9H_8ClN_2O]^+$, 193 $[C_9H_9N_2O_3]^+$, 165 $[C_8H_9N_2O_2]^+$, 150 $[C_8H_8NO_2]^+$, 139 $[C_7H_4ClO]^+$, 137 $[C_8H_9O_2]^+$, 111 $[C_6HCl]^+$, 109 $[C_6H_5O_2]^+$.

(E)-N'-[1-(2,4-Dihydroxyphenyl)ethylidene]-2,4-dichlorobenzohydrazide (**5e**)

Light brown amorphous solid; Yield: 86 %; m.p.: 178-180 ^oC; Mol. F.: $C_{15}H_{12}Cl_2N_2O_3$; Mol. mass: 338 $gmol^{-1}$; IR (KBr, υ_{max}/cm^{-1}): 3250 (O-H),

3041 (Ar C-H), 1672 (C=N), 1620 (Ar C=C); ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 7.91 (s, 1H, NH), 7.69 (d, J = 2.0 Hz, 1H, H-3'), 7.55 (d, J = 9.6 Hz, 1H, H-6), 7.35 (d, J = 9.4 Hz, 1H, H-5'), 7.19 (d, J = 8.0 Hz, 1H, H-6'), 6.91 (d, J = 9.5 Hz, 1H, H-5), 6.79 (s, 1H, H-3), 2.44 (s, 3H, CH_3-1"); EI-MS (*m/z*): 338 $[M]^+$, 323 $[C_{14}H_9Cl_2N_2O_3]^+$, 229 $[C_9H_7Cl_2N_2O]^+$, 193 $[C_9H_9N_2O_3]^+$, 173 $[C_7H_3Cl_2O]^+$, 165 $[C_8H_9N_2O_2]^+$, 150 $[C_8H_8NO_2]^+$, 145 $[C_6H_3Cl_2]^+$, 137 $[C_8H_9O_2]^+$, 109 $[C_6H_5O_2]^+$.

(E)-N'-[1-(2,4-Dihydroxyphenyl)ethylidene]-4-nitrobenzo hydrazide (**5f**)

Orange yellow amorphous solid; Yield: 85 %; m.p.: 232-234 ^{o}C; Mol. F.: $C_{15}H_{13}N_3O_5$; Mol. mass: 315 gmol^{-1}; IR (KBr, υ_{max}/cm^{-1}): 3254 (O-H), 3047 (Ar C-H), 1662 (C=N), 1619 (Ar C=C); ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 8.04 (d, J = 8.4 Hz, 2H, H-3' and H-5'), 7.95 (s, 1H, NH), 7.75 (d, J = 9.3 Hz, 1H, H-2' and H-6'), 7.50 (d, J = 9.6 Hz, 1H, H-6), 6.87 (d, J = 9.5 Hz, 1H, H-5), 6.88 (s, 1H, H-3), 2.45 (s, 3H, CH_3-1"); EI-MS (*m/z*): 315 $[M]^+$, 300 $[C_{14}H_{10}N_3O_5]^+$, 206 $[C_9H_8N_3O_3]^+$, 193 $[C_9H_9N_2O_3]^+$, 165 $[C_8H_9N_2O_2]^+$, 165 $[C_7H_5N_2O_3]^+$, 150 $[C_8H_8NO_2]^+$, 150 $[C_7H_4NO_3]^+$, 137 $[C_8H_9O_2]^+$, 122 $[C_6H_5NO_2]^+$, 109 $[C_6H_5O_2]^+$.

(E)-N'-[1-(2,4-Dihydroxyphenyl)ethylidene] phenylcarboxylatohydrazide (**5g**)

Yellow amorphous solid; Yield: 79 %; m.p.: 158-160 ^{o}C; Mol. F.: $C_{15}H_{14}N_2O_4$; Mol. mass: 286 gmol^{-1}; IR (KBr, υ_{max}/cm^{-1}): 3249 (O-H), 3047 (Ar C-H), 1657 (C=N), 1609 (Ar C=C); ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 8.01 (s, 1H, NH), 7.55 (d, J = 9.5 Hz, 1H, H-6), 7.45 (dd, J = 8.4 Hz, 2H, H-3' and H-5'), 7.25 (d, J = 9.6 Hz, 2H, H-2' and H-6'), 7.21 (dt, J = 8.1 Hz, 2.0 Hz, 1H, H-4'), 6.81 (d, J = 9.4 Hz, 1H, H-5), 6.87 (s, 1H, H-3), 2.40 (s, 3H, CH_3-1"); EI-MS (*m/z*): 286 $[M]^+$, 271 $[C_{14}H_{11}N_2O_4]^+$, 193 $[C_9H_9N_2O_3]^+$, 177 $[C_9H_9N_2O_2]^+$, 165 $[C_8H_9N_2O_2]^+$, 150 $[C_8H_8NO_2]^+$, 137 $[C_8H_9O_2]^+$, 121 $[C_7H_5O_2]^+$, 109 $[C_6H_5O_2]^+$.

(E)-N'-[1-(2,4-Dihydroxyphenyl) ethylidene]thiophene-2-carbohydrazide (**5h**)

Yellow amorphous solid; Yield: 78 %; m.p.: 240-242 ^{o}C; Mol. F.: $C_{13}H_{12}N_2O_3S$; Mol. mass: 276 gmol^{-1}; IR (KBr, υ_{max}/cm^{-1}): 3248 (O-H), 3049 (Ar C-H), 1669 (C=N), 1610 (Ar C=C); ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 8.42 (d, J = 8.4 Hz, 1H, H-3'), 8.11 (d, J = 8.6 Hz, 1H, H-5'), 7.91 (s, 1H, NH), 7.55 (d, J = 9.5 Hz, 1H, H-6), 7.50 (t, J = 8.4 Hz, 1H, H-4'), 6.88 (d, J = 9.5 Hz, 1H, H-5), 6.81 (s, 1H, H-3), 2.44 (s, 3H, CH_3-1"); EI-MS (*m/z*): 276 $[M]^+$,193 $[C_9H_9N_2O_3]^+$, 171 $[C_7H_{11}N_2OS]^+$, 165 $[C_8H_9N_2O_2]^+$, 150 $[C_8H_8NO_2]^+$, 137 $[C_8H_9O_2]^+$, 115 $[C_5H_7OS]^+$, 109 $[C_6H_5O_2]^+$.

(E)-N'-[1-(2,4-Dihydroxyphenyl) ethylidene]morpholine-4-carbohydrazide (**5i**)

Yellow amorphous solid; Yield: 88 %; m.p.: 312-314 ^{o}C; Mol. F.: $C_{13}H_{17}N_3O_4$; Mol. mass: 279 gmol^{-1}; IR (KBr, υ_{max}/cm^{-1}): 3243 (O-H), 3048 (Ar C-H), 1660 (C=N), 1616 (Ar C=C); ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) 7.95 (s, 1H, NH), 7.51 (d, J = 9.6 Hz, 1H, H-6), 6.89 (d, J = 9.6 Hz, 1H, H-5), 6.84 (s, 1H, H-3), 4.02-9.98 (m, 4H, CH_2-3 and CH_2-5), 3.50 (m, 4H, CH_2-2 and CH_2-6), 2.45 (s, 3H, CH_3-1"); EI-MS (*m/z*): 279 $[M]^+$, 193 $[C_9H_9N_2O_3]^+$, 170 $[C_7H_{12}N_3O_2]^+$, 165 $[C_8H_9N_2O_2]^+$, 150 $[C_8H_8NO_2]^+$, 137 $[C_8H_9O_2]^+$, 114 $[C_5H_8NO_2]^+$, 109 $[C_6H_5O_2]^+$.

Enzyme Inhibition Assay

α-Glucosidase Assay

The *α*-glucosidase inhibition activity was performed according to the method reported by Chapdelaine *et al.* [18]. All experiments were carried out in duplicates. The percent inhibition was calculated by the following equation,

$$\text{Inhibition (\%)} = \frac{\text{Control} - \text{Test}}{\text{Control}} \times 100$$

Butyrylcholinesterase Assay

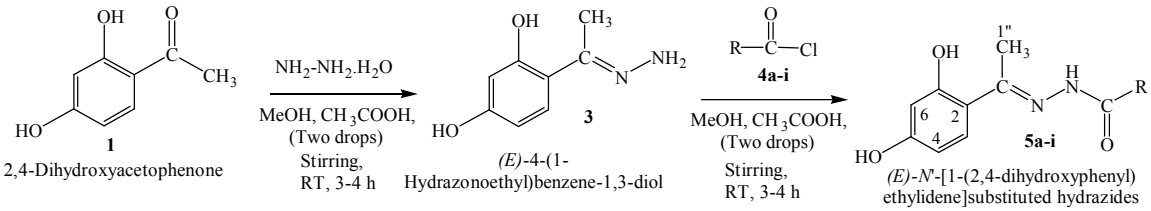
The BChE inhibition activity was performed according to the reported method [19] and the percent inhibition was calculated by the same formula as mentioned above.

Statistical Analysis

The results are presented as mean ± SEM for triplicate calculations after statistical analysis executed by MS Excel 2010.

Results and Discussion

(E)-N'-[1-(2,4-Dihydroxyphenyl)ethylidene]substituted hydrazides (**5a-i**), have been synthesized from 2,4-dihydroxyacetophenone (**1**) in two steps. The compounds were tested for enzyme inhibition activity against *α*-glucosidase and butyrylcholinesterase enzymes and were found to be decent inhibitors of butyrylcholinesterase enzyme [Table-2].



1 2,4-Dihydroxyacetophenone

3 *(E)*-4-(1-Hydrazonoethyl)benzene-1,3-diol

5a-i *(E)-N'*-[1-(2,4-dihydroxyphenyl) ethylidene]substituted hydrazides

Scheme-1: Synthesis of *(E)-N'*-[1-(2,4-dihydroxyphenyl)ethylidene]substituted hydrazides (**5a-i**).

Table-1: Acid halides (**4a-i**) used in the synthesis of *(E)-N'*-[1-(2,4-dihydroxyphenyl)ethylidene]substituted hydrazides (**5a-i**)

Comp.	R	Comp.	R	Comp.	R
5a	—CH3	**5d**		**5g**	—O—
5b	—CH2—Br	**5e**		**5h**	
5c		**5f**	—NO2	**5i**	—N

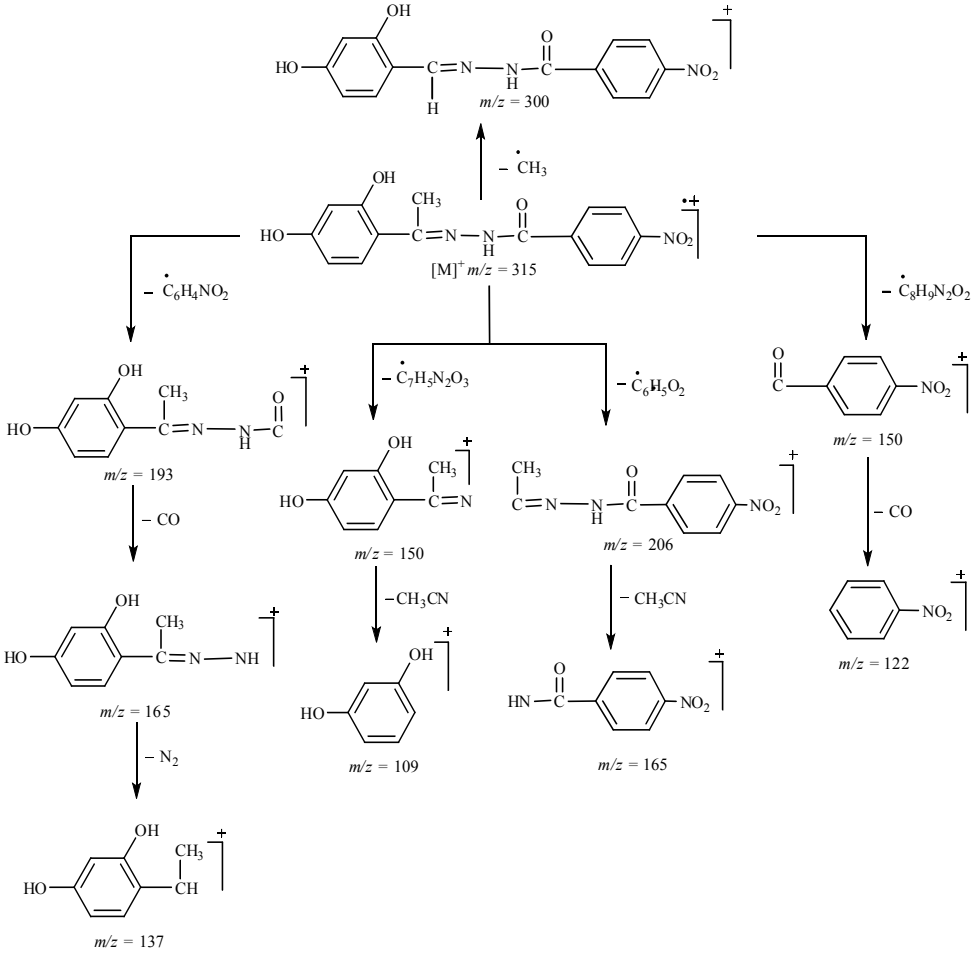


Fig. 1: Suggested mass fragmentation pattern of *(E)-N'*-[1-(2,4-Dihydroxyphenyl)ethylidene]-4-nitrobenzo hydrazide (**5f**).

Chemistry

In the first step 2,4-dihydroxyacetophenone (**1**) was converted to *(E)*-4-(1-hydrazonoethyl)benzene-1,3-diol (**3**) on stirring with hydrated hydrazine 80 % (**2**) in methanol and separated *i.e*. filtration after addition of excess of distilled water. The parent compound (**3**) was subjected to reaction with different acid halides (**4a-i**) in methanol in acidic conditions generated by glacial acetic acid. The synthesized derivatives (**5a-i**) were then separated by filtration after adding excess of distilled water. The respective details of appropriate procedures accompanied by spectral data are discussed in experimental section and elaborated in Scheme-1 and Table-1. The structures of various derivatives were analyzed through IR, ^{1}H-NMR and EI-MS spectroscopic data in same way for all the synthesized compounds.

Among substituted hydrazides, **5a-I**, one of the compounds **5f** is discussed in detail hereby for the expediency of the readers. Its molecular formula $C_{15}H_{13}N_3O_5$ was established by molecular ion peak at *m/z* 315, by mass spectrum and proton NMR by counting the number of protons. The prominent stretching frequencies in IR spectrum was observed at 3254 (O-H), 3047 (Ar C-H), 1662 (C=N), 1619 (Ar C=C). The base peak in mass fragmentation pattern was originated at *m/z* 150 for 4-(1-iminoethyl)-1,3-benzenediol cation and at *m/z* 300 for *N*-(2,4-dihydroxybenzylidine)-4-nitrobenzohydazide fragments. The other proposed prominent mass fragments are showed in Fig. 1. In the aromatic region of PNMR spectrum two doublets appeared at δ 8.04 (d, J = 8.4 Hz, 2H, H-3' and H-5') and δ 7.75 (d, J = 9.3 Hz, 2H, H-2' and H-6') for 4-nitrophenyl moiety, a singlet appeared at 7.95 for amide proton while for 1-(2,4-dihydroxyphenyl)-1-ethanone four signals appeared at δ 7.50 and δ 6.87 as doublets having J = 9.6 Hz, for 2 protons positioned at 6 and 5 respectively. A singlet for H-3 proton resonated at δ 6.88. In the aliphatic region a singlet appeared at δ 2.45 for (CH_3-1") having integration of 3 protons. The compound (**5f**) was designated as *(E)-N'*-[1-(2,4-dihydroxyphenyl)ethylidene]-4-nitrobenzo hydrazide. The structures of other synthesized molecules were also elucidated likewise.

Enzyme Inhibition Activity (in vitro)

The anti-enzymatic data against α-glucosidase enzyme revealed that compound **5i** exhibited acceptable IC_{50} value (127.13±0.86 µM) relative to standard Acarbose (38.25±0.12 µM) and **5b** also exhibited moderate IC_{50} value 157.18±0.87 µM as compared to reference standard. The order the inhibition observed for compounds synthesized was observed to be as **5i>5b>5a>6g>5c>5e**. The investigation of all synthesized compounds against butyrylcholinesterase (BChE) enzyme revealed that **5c** and **5g** showed decent inhibitory potential, having IC_{50} value, 31.74±0.08 µM, and 52.68±0.09 µM, respectively, relative to Eserine, a reference standard having IC_{50} value of 0.85±0.0001µM. The data is showed in Table-2.

Table-2: Enzyme Inhibition study on α-glucosidase and butyrylcholinesterase enzymes by synthesized *(E)-N'*-[1-(2,4-dihydroxyphenyl) ethylidene] substituted hydrazides (**5a-i**).

Compd.	Enzyme Inhibition Studies			
	α-Glucosidase		Butyrylcholinesterase	
	Inhibition (%) 0.5 mM	IC_{50} µM	Inhibition (%) 0.5 mM	IC_{50} µM
5a	90.85±1.13	179.81±0.94	60.41±1.57	175.38±0.95
5b	95.63±1.21	157.18±0.87	77.13±1.11	172.26±0.87
5c	77.28±2.13	402.24±1.18	88.45±0.72	31.74±0.08
5d	14.65±1.03	-	94.16±1.15	106.95±0.79
5e	57.28±1.53	426.51±1.01	-	
5f	13.59±0.97	-	18.09±0.32	-
5g	97.43±1.34	334.57±0.97	89.13±0.53	52.68±0.09
5h	4.37±0.56	-	5.78±0.04	-
5i	96.76±1.05	127.13±0.86	32.77±1.05	-
Control	92.23±0.14[a]	38.25±0.12[a]	82.82±1.09[b]	0.85±0.0001[b]

Note: IC_{50} values (concentration at which there is 50% enzyme inhibition) of compounds were calculated using EZ–Fit Enzyme kinetics software (Perella Scientific Inc. Amherst, USA). Also, **a** = Acarbose, **b** = Eserine

Conclusion

The synthesized compounds (**5a-i**) were analyzed for anti-enzymatic activity against α-glucosidase and butyrylcholinesterase enzymes and were found to be moderate inhibitors of butyrylcholinesterase enzyme. Moreover, this study also urges the researchers to investigate such molecules against various other enzymes to explore their therapeutic potentials for the ailment of diseases.

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