Original Research Article

Synthesis of Sulfanoquinoxaline-2,3-dione hydrazone Derivatives As a selective inhibitor for Acetylcholinesterase and Butyryl cholinesterase.

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Abstract

Some Sulfanoquinoxaline-2,3-diones hydrazone derivatives **(1-8)** were synthesized from the reactions of 2,3-dioxoquinoxaline-6-sulfonohydrazine with seven substituted benzaldehydes and acetophenone. All the synthesized compounds were biologically evaluated against cholinesterase's (acetylcholinesterase and butyryl cholinesterase). Compounds 1-8 were found to be a good selective inhibitor for acetylcholinesterase and butyryl cholinesterase. Among the series, compounds 3 (IC_{50} = 75 ± 10 µg/mL) and 5 (IC_{50} = 80 ± 10 µg/mL) were found to be the most active inhibitors against acetylcholinesterase, while compounds 6 (IC_{50} = 110 ± 10 µg/mL), 8 (IC_{50} = 130 ± 10 µg/mL) and 7 (IC_{50} = 150 ± 10 µg/mL), were found to be most active inhibitor against butyryl cholinesterase. The IC_{50} values for all the synthesized compounds were lower than standard, eserine (IC_{50} = 70 ± 20 µg/mL). Their considerable acetylcholinesterase and butyryl cholinesterase inhibitory activities makes them a good candidate for the development of selective acetylcholinesterase and butyryl cholinesterase inhibitors.

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Keywords: Alzheimer's disease, acetylcholine, quinoxaline, acetylcholinesterase, butyrylcholinesterase, eserine, hydrazone

INTRODUCTION

Heterocycles containing quinoxaline derivatives have gained considerable attention from researchers in recent years. Quinoxaline and its numerous derivatives have been widely reported because of their biological activity, specifically as antimicrobial (Badran *et al*., 2003; Jaso *et al*., 2003; Hearn and Cynamon 2004; Kaurase *et al.*, 2011; Aswartha *et al*., 2012; Achutha *et al.*, 2013), antibacterial (Bailly *et al*.,1999; Burguete *et al*., 2007; Beheshtiha *et al.*, 2010), anti-cancer (Chen *et al*., 2004), antiaminoceptive (Deepika and Nath, 2012), anti-inflammatory (Wagle *et al*., 2008; Rajitha *et al*., 2011) anti-viral (Michael *et al*., 2002; Lindsley *et al*., 2005; Geefhavani *et al*., 2012), antimalaria (Rangisetty *et al*., 2001) agents. Alzheimer's disease (AD) is a common form of dementia in which severe loss of cholinergic cells occurs, which subsequently leads to low levels of the neurotransmitter Acetylcholinesterase (Ach) in the brain, while activity of BChE does not change or even elevate in advanced AD, which suggests a key involvement of BChE in ACh hydrolysis during AD symptoms. Such neurological changes in the nervous system may contribute to various cognitive and behavioral symptoms that appear during AD. Therefore, inhibiting the activity of BChE may be an effective way to control AD associated disorders.

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MATERIALS AND METHODS

General

Melting points were determined with open capillary tube on a Gallenkamp (variable heater) melting point apparatus and were uncorrected. Infrared spectra were recorded as KBr pellets on a Buck Spectrometer. The ^{1}H and ^{13}C NMR was run on a Bruker 600 MHz spectrometer (δ in ppm relative to Me_4Si), The purity of the compounds were routinely checked by TLC on silica gel G

plates using n-hexane/ethyl acetate (1:1, v/v) solvent system and the developed plates were visualized by UV light. All reagents used were obtained from Sigma–Aldrich Chemical Ltd, except Glacial acetic acid, ethanol, oxalic acid and vanillin which were obtained from BDH Chemical Limited.

Synthesis of quinoxaline-2,3-(1H,4H)-dione-6-sulfonyl hydrazide 1

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Hydrazine hydrate (10 ml, 0.460 mmol) in absolute methanol (100 mL) was added quinoxaline-6-sulfonylchloride (15 g, 0.55 mol) portion wise with constant stirring. The reaction mixture obtained was refluxed at 80 °C for 4 hours. The solution was cooled and poured into crushed ice to give **1′.** Melting point >330 °C. **IR Spectra (KBr)** 3347 cm^{-1} (N-H), 3139 cm^{-1} (N-H), 3050 cm^{-1} (N-H), 3039 cm^{-1} (N-H), 1669 cm^{-1} (C=O), 1595 cm^{-1} (C=N), 1391 (SO_2), 1159 cm^{-1} (SO_2). **^{1}H NMR (DMSO-d_6)** 3.37 (br s, 1H, NH, D_2O exchangeable), 4.12 (br s, 1H, NH, D_2O exchangeable), 12.10 (br s, 1H, NH, D_2O exchangeable), 8.37 (br s, 1H, NH, D_2O exchangeable), 7.60 (d, 1H, ArH), 7.49-7.50 (dd, 1H, ArH), 7.27 (d, 1H, ArH. **^{13}C NMR (DMSO-d_6)** 154.86 (C=O), 131.98 (Aromatic), 128.95 (Aromatic), 125.50 (Aromatic), 122.33 (Aromatic), 115.27 (Aromatic), 114.96 (Aromatic)

Synthesis of N-(E)-(phenylideneamino)-6-(quinoxaline-2,3-(1H,4H)-dione)sulfonamide 1-6

A mixture of Quinoxaline-6-sulfonohydrazine 1 (39 mmol), the required benzaldehydes (39 mmol) and glacial acetic acid (25 mL was refluxed at 120 °C for 3 hours. The resulting mixture was cooled and poured into crushed ice with continuous stirring. The solid obtained was filtered and washed with cold water, dried and recrystallized from DMF/water to afford the desired product.

N-(E)-(3-Chlorobenzylideneamino)-6-(quinoxaline-2,3-(1H,4H)-dione)sulfonamide 1

A yellow solid, m.p 239-240ºC, lit. 241-243 ºC (Taiwo and Obafemi, 2016)**. IR Spectra (KBr)**: 3238 cm^{-1} (N-H), 3215 cm^{-1} (N-H), 3042 cm^{-1} (CH aromatic), 1692 cm^{-1} (C=O), 1603 cm^{-1} (C=N), 1371 ($\nu_{max}SO_2$), 1163 cm^{-1} (SO_2). **^{1}H NMR (DMSO-d_6)** 12.12 (br s, 2H, NH, D_2O exchangeable), 11.61 (br s, 1H, NH, D_2O exchangeable), 7.89 (s, 1H, ArH), 7.66 (d, 1H, ArH), 7.24 (d, 1H, ArH), 7.44 (m, 2H, ArH), 7.56 (m, 2H, ArH), 8.72 (s, 1H, N=CH). **^{13}C NMR (DMSO-d_6)**: 160.58 (C=O), 155.18 (C=O), 154.92 (C=N), 145.79, 134.54 (Aromatic), 132.53 (Aromatic), 132.66 (Aromatic), 130.00 (Aromatic), 129.52 (Aromatic), 129.07 (Aromatic), 128.84 (Aromatic), 128.45 (Aromatic), 125.85 (Aromatic), 121.97 (Aromatic), 115.42 (Aromatic), 114.20 (Aromatic).

N-(E)-(3-nitrobenzylideneamino)-6-(quinoxaline-2, 3-(1H, 4H)-dione)sulfonamide 2

A yellow solid, m.p 249-251ºC, lit.250 ºC (Taiwo and Obafemi, 2016)**.IR Spectra (KBr)**: 3247 cm^{-1} (N-H), 3239 cm^{-1} (N-H), 3077 cm^{-1} (CH aromatic), 1680 cm^{-1} (C=O), 1599 cm^{-1} (C=N), 1341 cm^{-1} ($\nu_{max}SO_2$), 1151 cm^{-1} (SO_2). **^{1}H NMR (DMSO-d_6)**: 12.20 (br s, 1H, NH, D_2O exchangeable), 12.13 (br s, 1H, NH, D_2O exchangeable), 12.00 (br s, 1H, NH, D_2O exchangeable), 8.27 (d, 1H, ArH), 8.15 (dd, 2H, ArH), 7.58 (dd, 1H, ArH), 7.26-7.28 (d, 1H, ArH), 7.66 (m, 1H, ArH), 6.76(m, 1H, ArH) , 8.97 (s, 1H, N=CH). **^{13}C NMR (DMSO-d_6)**: 158.65 (C=O), 155.19 (C=O), 154.91 (C=N), 148.85 (Aromatic), 147.85 (Aromatic), 133.91 (Aromatic), 133.75 (Aromatic), 132.14 (Aromatic), 129.63 (Aromatic), 129.41 (Aromatic), 127.94 (Aromatic), 127.79 (Aromatic), 125.93 (Aromatic), 124.76 (Aromatic), 124.65 (Aromatic), 115.55 (Aromatic), 114.20 (Aromatic).

N-(E)-(4-methoxybenzylideneamino)-6-(quinoxaline-2,3-(1H,4H)-dione)sulfonamide 3

A yellow solid, m.p 260-262^{o}C, lit. 262-263 ^{o}C (Taiwo and Obafemi, 2016)**.IR Spectra (KBr)** 3486 cm^{-1} (N-H), 3212 cm^{-1} (N-H), 3062 cm^{-1} (CH aromatic), 1684 cm^{-1} (C=O), 1586 cm^{-1} (C=N), 1387 cm^{-1} (C-O), 1310 (SO_2), 1155 cm^{-1} (SO_2). **^{1}H NMR (DMSO-d_6)** 12.16 (br s, 2H, NH, D_2O exchangeable), 11.50(br s, 1H, NH, D_2O exchangeable), 7.80 (d, 1H, ArH), 7.58 (dd, 1H, ArH), 7.17 (d, 1H, ArH), 7.12 (m, 1H, ArH), 7.27 (dd, 1H, ArH), 7.32 (t, 1H. ArH), 6.96-6.98(m, 1H, ArH) 7.68 (s, 1H, N=CH), 3.78 (s, 3H, -OCH_3). **^{13}C NMR (DMSO-d_6)** 159.39 (C=O), 155.20 (C=O), 154.95 (C=N), 146.97 (Aromatic), 134.97 (Aromatic), 132.66 (Aromatic), 130.30 (Aromatic), 129.87 (Aromatic), 129.50 (Aromatic), 125.81 (Aromatic), 125.58 (Aromatic), 122.41 (Aromatic), 122.02 (Aromatic), 119.36 (Aromatic), 115.85 (Aromatic), 115.42 (Aromatic), 114.31 (Aromatic), 112.87 (Aromatic), 111.61 (Aromatic), 55.10 (CH_3).

N-(E)-(4-hydroxybenzylideneamino)-6-(quinoxaline-2,3-(1H,4H)-dione)sulfonamide 3

A yellow solid, m.p 240-242^{o}C, lit. 239-241 ^{o}C (Taiwo and Obafemi, 2016)**. IR Spectra (KBr)**: 3668 cm^{-1} (N-H), 3459 cm^{-1} (N-H), 3050 cm^{-1} (CH aromatic), 1684 cm^{-1} (C=O), 1599 cm^{-1} (C=N), 1395 cm^{-1} (C-O), 1322 (SO_2), 1151 cm^{-1} (SO_2). **^{1}H NMR (DMSO-d_6)**: 12.18 (br s, 1H, NH, D_2O exchangeable), 12.13 (br s, 1H, NH, D_2O exchangeable), 11.30 (br s, 1H, NH, D_2O exchangeable), 7.77 (d, 1H, ArH), 7.67 (d, 1H, ArH), 7.24 (dd, 1H, ArH), 7.52 (d, 2H, ArH), 6.94 (d, 2H, ArH), 8.64 (s, 1H, N=CH), 3.75 (s, 3H, -OCH_3). **^{13}C NMR (DMSO-d_6)**: 160.77 (C=O), 160.46 (C=O), 155.19, 154.94 (C=N), 147.17 (Aromatic), 132.81 (Aromatic), 129.94 (Aromatic), 129.40 (Aromatic), 128.43 (Aromatic), 126.51 (Aromatic), 126.19 (Aromatic), 125.77 (Aromatic), 122.01 (Aromatic), 115.35 (Aromatic), 114.35 (Aromatic), 114.31 (Aromatic), 114.19 (Aromatic), 55.23 (CH_3), 55.34 (CH_3).

Synthesis of N-(E)-((1-(4-dimethylamino)phenyl)methylideneamino)-6-(quinoxaline-2,3-(1H,4H)-dione)sulfonamide 5

Melting point 288-290 ºC lit 286-288 ºC [17] **IR Spectra (KBr)** 3193 cm^{-1} (N-H), 3135 cm^{-1} (N-H), 3035 cm^{-1} (CH aromatic), 1676 cm^{-1} (C=O), 1584 cm^{-1} (C=N), 1318 (SO_2), 1159 cm^{-1} (SO_2). **^{1}H NMR (DMSO-d_6)** 12.13 (br s, 1H, NH, D_2O exchangeable), 11.92 (br s, 1H, NH, D_2O exchangeable), 10.04 (br s, 1H, NH, D_2O exchangeable), 7.76 (s, 1H, ArH), 7.74 (d, 2H, ArH), 7.55 (ddd, 1H, ArH), 7.38-7.44 (dd, 2H, ArH), 7.23-7.32 (ddd, 1H, ArH), 8.61 (s, 1H, N=CH), 2.50 (s, 6H, CH_3). **^{13}C NMR (DMSO-d_6)**

155.18 (C=O), 154.92 (C=O), 137.27 (Aromatic), 132.79 (Aromatic), 132.05 (Aromatic), 129.72 (Aromatic), 129.40 (Aromatic), 129.02 (Aromatic), 128.40 (Aromatic), 128.34 (Aromatic), 126.44 (Aromatic), 126.01 (Aromatic), 125.66 (Aromatic), 125.58 (Aromatic), 122.40 (Aromatic), 14.67 (CH_3), 14.27 (CH_3)

Synthesis of N-(E)-((1-(4-methoxy-3-hydroxyl-)phenyl)ethylideneamino)-6-(quinoxaline-2,3-(1H,4H)-dione)sulfonamide 6

Melting point 230-231 ºC lit 233 ºC (decomposed)[17] **IR Spectra (KBr)** 3363 cm^{-1} (OH), 3239 cm^{-1} (N-H), 3054 cm^{-1} (CH aromatic), 1680 cm^{-1} (C=O), 1588 cm^{-1} (C=N), 1391 cm^{-1} (C-O), 1333 (SO_2), 1156 cm^{-1} (SO_2). **^{1}H NMR (DMSO-d_6)**

12.13 (br s, 2H, NH, D_2O exchangeable), 11.20 (br s, 1H, NH, D_2O exchangeable), 9.50 (s, 1H, ArH), 7.56-7.57 (dd, 1H, ArH), 7.66 (d, 1H, ArH), 6.98 (dd, 1H, ArH), 7.24-7.26 (d, 1H, ArH), 7.10 (d, 1H, ArH), 7.77 (s, 1H, N=CH), 3.78 (s, 6H, OCH_3)**. ^{13}C NMR (DMSO-d_6)** 154.89 (C=O), 148.79 (C=N), 147.73 (C-O), 132.72 (Aromatic), 129.32 (Aromatic), 125.68 (Aromatic),

124.96 (Aromatic), 121.99 (Aromatic), 121.08 (Aromatic), 115.35 (Aromatic), 115.29 (Aromatic), 114.31 (Aromatic), 109.50 (Aromatic), 55.47 (CH_3).

Synthesis of N-(E)-(7-chloro-2-oxoindole-3-ylideneamino)-6-(quinoxaline-2,3-(1H,4H)-dione)sulfonamide 7

Melting point 268-270 ºC lit 273-274 ºC [17]. **IR Spectra (KBr)** 3324 cm^{-1} (N-H), 3104 cm^{-1} (N-H), 1680 cm^{-1} (C=O), 1595 cm^{-1} (C=N), 1383 cm^{-1} (C-O), 1322 (SO_2), 1163 cm^{-1} (SO_2). **^{1}H NMR (DMSO-d_6)** 12.21 (br s, 1H, NH, D_2O exchangeable), 12.17 (br s, 1H, NH, D_2O exchangeable), 10.73 (br s, 1H, NH, D_2O exchangeable), 7.72 (d, 1H, ArH), 7.87 (d, 1H, ArH), 7.63-7.65 (dd, 1H, ArH), 6.85-6.86 (d, 1H, ArH), 7.27-7.29 (d, 1H, ArH), 7.37 (t, 1H, ArH), 7.06 (t, 1H, ArH). **^{13}C NMR (DMSO-d_6)** 171.93 (C=O), 163.61 (C=O), 155.16 (C=O), 154.86 (C=N), 143.84 (Aromatic),141.84 (Aromatic), 133.07 (Aromatic), 131.58 (Aromatic), 129.86 (Aromatic), 126.58 (Aromatic), 125.67 (Aromatic), 122.75 (Aromatic), 121.60 (Aromatic), 115.36 (Aromatic), 115.12 (Aromatic), 115.02 (Aromatic) 110.50 (Aromatic).

Synthesis of N-(E)-(-1-phenylethylideneamino)-6-(quinoxaline-2,3-(1H,4H)-dione)sulfonamide 8

Melting point 288-290 ºC lit 290-292 ^{0}C [17]. **IR Spectra (KBr)** 3347 cm^{-1} (N-H), 3139 cm^{-1} (N-H), 3039 cm^{-1} (CH aromatic), 2927 cm^{-1} (CH aliphatic) 1676 cm^{-1} (C=O), 1595 cm^{-1} (C=N), 1314 (SO_2), 1167 cm^{-1} (SO_2). **^{1}H NMR (DMSO-d_6)** 12.17 (br s, 2H, NH, D_2O exchangeable), 8.36 (br s, 1H, NH, D_2O exchangeable), 8.35 (s, 1H, ArH), 7.91 (m, 1H, ArH), 7.25 (d, 1H, ArH), 7.60 (d, 1H, ArH), 7.46 (m, 3H, ArH), 2.50 (s, 3H, CH_3). **^{13}C NMR (DMSO-d_6)** 158.56 (C=O), 155.12 (C=O) 154.88 (C=N), 151.13, 148.17 (Aromatic), 143.28 (Aromatic), 132.89

(Aromatic), 129.23 (Aromatic), 128.09 (Aromatic), 125.65 (Aromatic), 124.58 (Aromatic), 121.96 (Aromatic), 120.51 (Aromatic), 115.23 (Aromatic), 114.31 (Aromatic), 111.93 (Aromatic) 111.84 (Aromatic), 20.95 (CH_3).

In vitro acetylcholinesterase and butyrylcholinesterase Inhibitory Assays

The anti-cholinesterase (acetylcholinesterase and butyrylcholinesterase) inhibiting activities of the synthesized compounds were determined by using modified method of Ellman et al. (1961) as described by Obuotor (2004). The synthesized compounds were prepared in a stock solution of DMSO in buffer and was used for the cholinesterase inhibition assay, while Eserine prepared in buffer was used as the reference compound (positive control).

Procedure: To triplicate test tube was added 240µl of buffer (50 mM Tris-HCl, pH 8.0) and 20 µl of varying concentration of the test compounds (10, 5, 2.5 and 1.25 mg/ mL), 20µl of the enzyme preparation, the reaction mixture was then incubated for 30mins at 37^0C, after which 20 µl of 10 mM 5,5'-dithiobis (2-nitrobenzoic acid), was added.

The reaction was then initiated by the addition of 20µl of 25mM ATChI (1.042 mM final concentration). The rate of hydrolysis of ATChI was then determined spectrophotometrically by measuring the change in the absorbance per minute (ΔA/min) due to the formation of the yellow 5-thio-2-nitrobenzoate anion at 412 nm over a period of 4 min at 30s interval. A solution of buffer was used as negative control. The percentage inhibition (% I) of the synthesized compounds were obtained using the formula:

$$I\ (\%) = [(V_0 - V_i)/V_0]*100$$

Where: I (%) = Percentage inhibition

V_i = enzyme activity in the presence of synthesized compounds

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V_0 = enzyme activity in the absence of synthesized compounds

RESULTS AND DISCUSSION

Chemistry

The reactions of 2,3-dioxo-1,2,3,4-tetrahydroquinoxaline-6-sulfonyl hydrazide I with some aromatic aldehydes under refluxing condition in glacial acetic acid afforded the hydrazones 1 – 6 as shown in Scheme 1. Furthermore, N-(E)-(2-oxoindole-3-ylideneamino)-6-(quinoxaline-2,3-(1H,4H)-dione) sulfonamide 7 was prepared by the reaction of **I** with isatin as shown in Scheme 1. The reaction of **I** with acetophenone under refluxing condition in glacial acetic acid afforded the hydrazone 8. Generally, the infrared spectra of the compounds showed absorption bands due to the stretching vibrations of N-H and OH between 3135 and 3390 cm-1, C=O between 1676 and 1692 cm-1, C=C and C=N between 1607 and 1580 cm-1, SO_2 at 1310 - 1391 cm-1 and 1140 - 1167 cm-1 for asymmetric and symmetric vibrations. The 1H-NMR spectral data of compounds 1-8 in DMSO-d6 showed signal for NH between 8.37 ppm and 12.51 ppm, the signals for CH=N between 7.68-ppm and 9.59 ppm, the signals for aromatic protons were observed between 6.40 ppm and 9.50 ppm, the signals for methyl protons (CH3) were seen at 2.50 ppm and the signals for methoxy protons (OCH3) were observed between 3.75 ppm and 3.78 ppm.

SCHEME 1: Synthetic procedure for compounds 1-8

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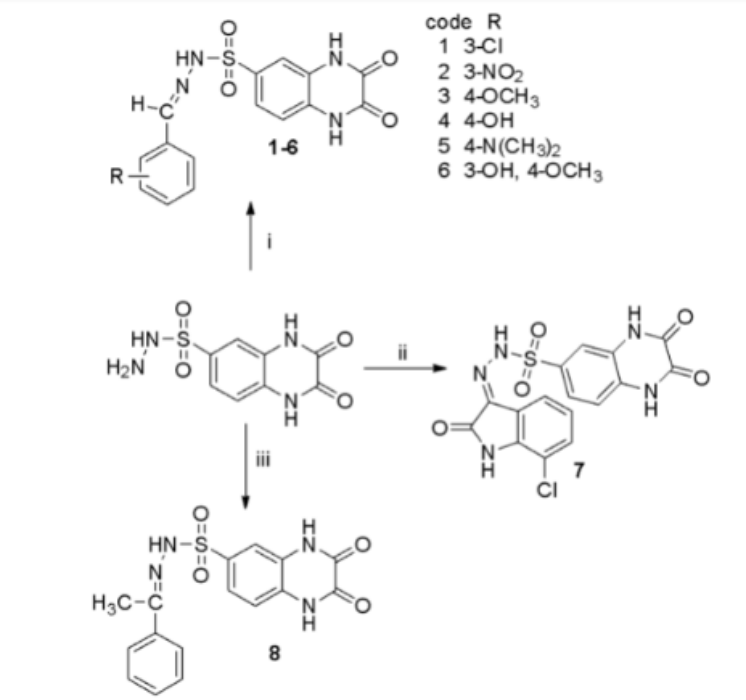

i. substituted benzaldehydes (2-7) ii) isatin (8) (iii) acetophenone (9). Reaction condition: glatial acetic acid, reflux at 120 0C.

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Biology

Alzheimer disease (AD) is one of the most ordinary neurodegenerative diseases resulting in progressive dysfunction in the brain which has become a major health problem among the aged all over the world. Alzheimer disease brains show extensive cell loss, particularly of cholinergic neurons (Sultan 2013), and reduction of the neurotransmitter acetylcholine, producing the cholinergic dysfunction characteristic of AD (Sultan 2013).

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It is also established that AChE levels decrease in AD, while BuChE activity does not (Darvesh 2010). BuChE co-regulates acetylcholine metabolism as demonstrated by the fact that AChE-knockout mice are viable (Mesulam 2002). The accumulation of BuChE in AD pathology

is especially notable in cortical grey matter, an area that normally has very little BuChE activity (Sultan 2013). Therefore, inhibition of both acetylcholinesterase (AChE) and butyrylcholinesterace (BChE), the enzymes responsible for hydrolysis of ACh at the cholinergic synapse and grey matter respectively, is currently the most established approach for treating AD (Coyle et al., 1973).

The present study established that the synthetic compounds show a dual inhibition of both AChE and BChE, with more preference to BChE. All the tested compounds exhibit a very strong inhibition towards BChE more than AChE as observed from their $IC_{50.}$ This might be as a result of larger size of the compounds which makes them fit properly into the active site of BChE more than AChE, thereby resulting into higher inhibition.

The results also established that compounds 1, 2, 5, 6, 7 and 8 have a higher inhibitory activity towards BChE when compared to the reference compound i.e. eserine, which shows that they can serve as a potent and lead compounds which can be optimized for treatment of AD

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A study also demonstrated that selective BuChE inhibitors reduced amyloid precursor protein processing and Aβ level *in vivo* and *in vitro* (Arif et al., 2012). These results suggest that the effects may arise from the interaction of these compounds with amyloid cascade, influencing the expression and metabolic processing of APP and thereby slowing down the major pathological consequences of aggregation (Mukherjee et al., 2007). Therefore, cholinesterase inhibitors not only increase the level of ACh but also prevent the formation of β-amyloidal plaques thereby protecting the neurons from neurodegeneration.

Conclusion

The results obtained from this study clearly indicate that the synthesized compounds have a potent cholinesterase inhibitory activity under *in vitro* study. The most probable reason for their potential ChEI activity might be related to their large size and chemical structure. This can be further characterized, and they can be evaluated for their bioavailability and potential toxicity *in vivo*.

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COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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Comment [a35]: Replace , by ;

Comment [a36]: Replace , by ;

Comment [a37]: Use similar format in the title .

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Compounds						
	Inhibition (%) at 0.5 mM	IC_{50} lM ± SEM[a]	Inhibition (%) at 0.5 mM	IC_{50} lM ± SEM[a]	AChE[c]	BChE[c]
1	68.76	0.9 ±0.10	70.87	1.51±0.1	1.68	0.60
2	78.71	1.48±0.25	68.8	1.73±0.04	1.17	0.86
3	66.49	0.75±0.01	75.98	5.0±0.37	6.67	0.15
4	63.62	1.00±0.02	75.73	5.61±0.10	5.61	0.18
5	64.29	0.80±0.01	80.2	1.60±0.01	1.63	0.61
6	63.05	0.98±0.01	90.74	1.10±0.01	1.38	0.72
7	76.34	0.88±0.01	87.86	1.50±0.01	1.70	0.59
8	70.2	1.28±0.01	88.84	1.30±0.01	1.01	0.98
Eserine[b]	68	0.07±0.02	99.65	2.70±0.03	38.57	0.026

Table 1: Bioactivity studies results for sulfonamides (1–8)

a All reactions were performed in triplicates and averaged, and SEM is standard mean error of the experiments, b Standards used, c selectivity for AChE = BChE/AChE; selectivity for BChE = AChE/BChE

Figure 1: Inhibition (%) of AChE by Compounds 1-8

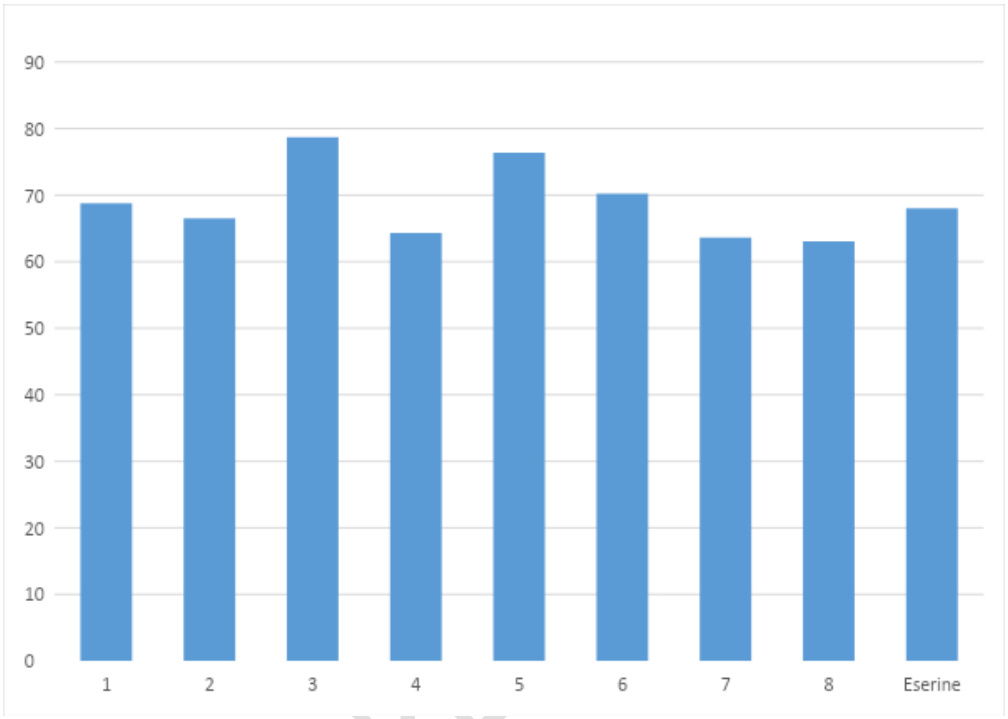

Figure 2: Inhibition (%) of BChE by Compounds 1-8

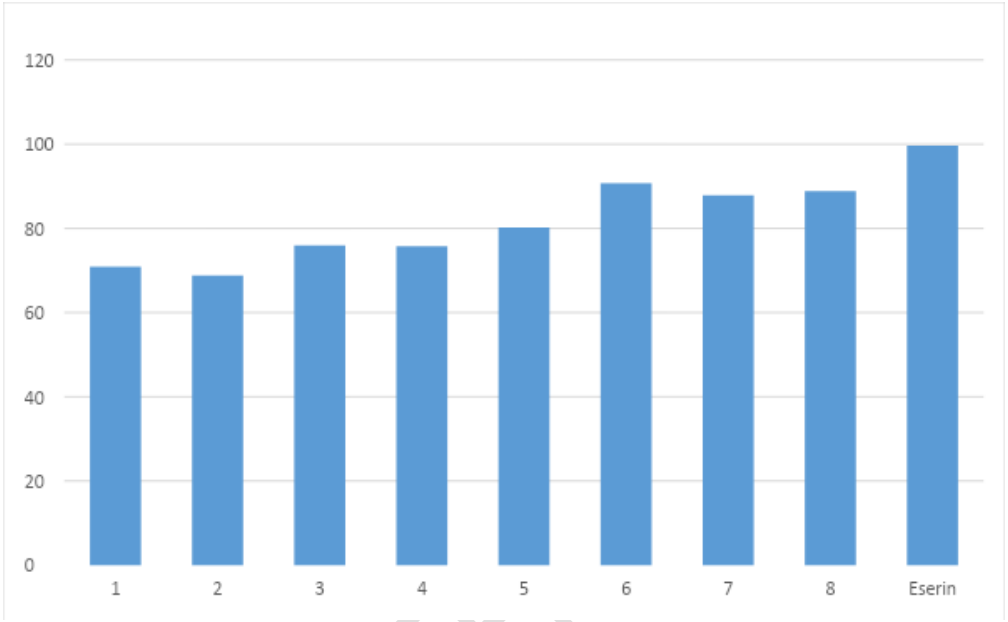

Figure 3: IC_{50} of AChE by Compounds 1-8

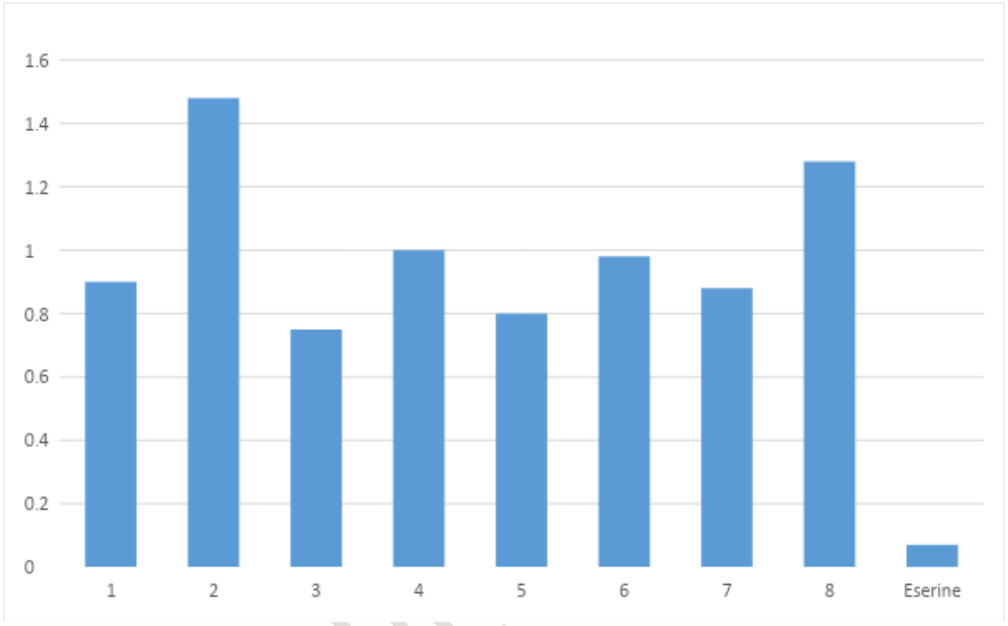

Figure 4: IC_{50} of BChE by Compounds 1-8