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DESIGN AND SYNTHESIS OF BENZOFURAN LINKED CHALCONE HYBRIDS AS POTENTIAL ANTIDIABETIC AGENTS

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ABSTRACT

Chalcones are an important class of bioactive compounds known for their diverse pharmacological properties, while benzofuran derivatives are recognized as valuable scaffolds in medicinal chemistry due to their wide range of biological activities. In the present study, a series of novel benzofuran-containing chalcone derivatives were synthesized and evaluated for their pharmacological potential. The target compounds were prepared via Claisen–Schmidt condensation by reacting 2-acetylbenzofuran with various substituted aromatic aldehydes in the presence of ethanolic sodium hydroxide under mild reaction conditions. The synthesized compounds were obtained in good yields and purified by recrystallization. Structural elucidation of the synthesized derivatives was carried out using physicochemical and spectroscopic techniques, including M.P, elemental analysis, IR spectroscopy, ¹H NMR, ¹³C NMR, and mass spectrometry, confirming the formation of the desired benzofuran–chalcone framework.

The synthesized compounds were further subjected to pharmacological evaluation using appropriate *in vitro* biological assays. The results revealed that several derivatives exhibited notable pharmacological activity, which may be attributed to the presence of both benzofuran and chalcone pharmacophores within the same molecular framework. Overall, the findings of the present study suggest that benzofuran-based chalcone derivatives represent promising candidates for further investigation as potential antidiabetic agents and may serve as useful lead structures in the development of new therapeutic molecules.

Key words: Chalcone, Benzofuran, Diabetis, Spectral studies, Claisen–Schmidt condensation

INTRODUCTION

Chalcones are an important class of naturally occurring and synthetic compounds belonging to the flavonoid family, characterized by the presence of an α,β -unsaturated carbonyl system linking two aromatic rings. They serve as key intermediates in the biosynthesis of flavonoids and isoflavonoids and have attracted considerable attention in medicinal chemistry due to their broad spectrum of biological activities. Benzofuran derivatives exhibit diverse pharmacological activities such as antimicrobial [1], anti-inflammatory [2], anticancer [3, 4], antibacterial [5], antitubercular [6], neurodisorders [7, 8] and antidiabetic properties [9, 10], antiviral [11], antioxidant [12, 13] and antihypertensive [14]. Among heterocyclic scaffolds, the benzofuran nucleus represents an important structural motif frequently found in natural products and biologically active molecules.

In recent years, molecular hybridization has emerged as an effective strategy in drug design, wherein two pharmacologically active scaffolds are combined within a single molecule to enhance biological efficacy. In this context, benzofuran–chalcone hybrids have gained considerable attention due to the presence of both the benzofuran heterocyclic nucleus and the biologically active chalcone pharmacophore, which may contribute to

improved pharmacological potential. Moreover, diabetes mellitus, a chronic metabolic disorder characterized by persistent hyperglycemia, remains a major global health concern, prompting the search for novel therapeutic agents capable of controlling blood glucose levels. One promising approach involves the inhibition of carbohydrate-digesting enzymes such as α -amylase and α -glucosidase, which play key roles in postprandial glucose regulation. Therefore, the present study focuses on the synthesis of novel benzofuran-based chalcone derivatives via Claisen–Schmidt condensation, followed by their structural characterization and evaluation of their antidiabetic activities using standard *in-vitro* assays, with the aim of identifying potential lead molecules for the development of new therapeutic agents.

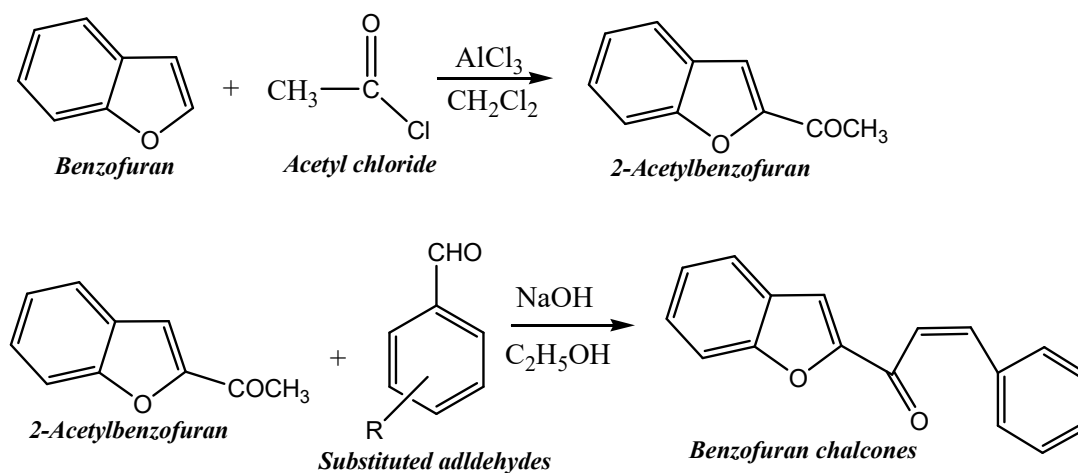
Synthesis of benzofuran chalcone derivatives:

Benzofuran (0.01 mol) with acetyl chloride (0.012 mol) in the presence of anhydrous AlCl_3 (0.012 mol) in dichloromethane (20 mL) at 5 $^{\circ}\text{C}$. A mixture of 2-acetylbenzofuran (0.01 mol) and substituted benzaldehydes (0.01 mol) in ethanol (25 mL) were added. Place all the vials into the parallel synthesizer block and stir the reaction mixture at room temperature (25–30 $^{\circ}\text{C}$) for 10–15 hours. The

progress of each reaction is monitored periodically by Thin Layer Chromatography (TLC) using a suitable solvent chloroform: methanol (9:1). Pour the reaction mixture into ice-cold distilled water (50–70 mL). Acidify with dilute hydrochloric acid, A yellow precipitate of benzofuran chalcone separates

out. Filter the precipitated product using vacuum filtration and wash with cold water to remove residual base and impurities. The crude product is purified by recrystallization from ethanol or ethanol–water mixture to afford the benzofuran chalcone derivatives.

Scheme: Synthesis of benzofuran chalcone derivatives



1-(Benzofuran-2-yl)-3-phenylprop-2-en-1-one (BC-1): Yellow crystalline solid; Yield: 78%; M.P: 114–116 °C. Mass spectrum (ESI-MS): m/z 248 (M^+) corresponding to the molecular ion peak of $\text{C}_{17}\text{H}_{12}\text{O}_2$; fragment ions observed at 247 ($\text{M}-\text{H}$), 219 ($\text{M}-\text{CHO}$), 191 (benzofuran fragment), 165 (phenyl-CO fragment), and 105 (benzoyl ion, $\text{C}_6\text{H}_5\text{CO}^+$). IR (KBr, ν_{max} , cm^{-1}): 3062 (aromatic C–H stretching), 1656 (α,β -unsaturated C=O stretching of chalcone), 1602 and 1587 (aromatic C=C stretching), 1512 (conjugated C=C), 1450 (C–H bending), 1252 (C–O–C stretching of benzofuran ring), 1178, 1025

(C–O stretching), 758 and 701 (aromatic C–H out-of-plane bending).

The ^1H NMR (400 MHz, CDCl_3 , δ ppm): 8.02 (d, 1H, $J = 15.6$ Hz, H- β , $\text{CH}=\text{CH}-\text{CO}$), 7.85 (d, 1H, $J = 15.6$ Hz, H- α , $\text{CH}=\text{CH}-\text{Ph}$), 7.74–7.71 (m, 1H, benzofuran Ar-H), 7.68 (d, 1H, benzofuran Ar-H), 7.60–7.52 (m, 3H, phenyl Ar-H), 7.46–7.38 (m, 3H, aromatic H), 7.31 (d, 1H, benzofuran Ar-H), 7.27 (t, 1H, aromatic H). The coupling constant ($J \approx 15$ –16 Hz) confirms the trans configuration of the α,β -unsaturated system.

The ^{13}C NMR (100 MHz, CDCl_3 , δ ppm): 188.6 (C=O, chalcone carbonyl), 154.4

(benzofuran C–O), 146.7 (β -carbon of C=C), 138.8, 134.6, 131.3, 129.9, 128.7, 128.4, 127.8, 126.6, 124.9, 123.5, 122.1, 119.7, 112.6 (aromatic and olefinic carbons of benzofuran and phenyl rings).

1-(Benzofuran-2-yl)-3-(4-hydroxyphenyl)prop-2-en-1-one (BC-2):

Yellow crystalline solid; Yield: 76%; M.P: 168–170 °C. Elemental Analysis: Calculated for $C_{17}H_{12}O_3$: C, 77.26; H, 4.58%. Found: C, 77.18; H, 4.62%. MS (ESI-MS): m/z 264 (M^+) corresponding to molecular ion peak; fragments observed at 263 ($M-H$), 235 ($M-CO$), 191 (benzofuran fragment), 165 (aryl carbonyl fragment), 105 (benzoyl ion).

IR (KBr, ν_{max} cm^{-1}): 3428 (phenolic O–H stretching), 3060 (aromatic C–H stretching), 1655 (α,β -unsaturated carbonyl C=O stretching of chalcone), 1602 and 1584 (aromatic C=C stretching), 1512 (conjugated C=C), 1452 (C–H bending), 1250 (phenolic C–O stretching), 1178 (C–O vibration), 758 and 701 (aromatic C–H out-of-plane bending).

The ^1H NMR (400 MHz, $CDCl_3$, δ ppm): 8.01 (d, 1H, $J = 15.6$ Hz, H- β of $CH=CH-CO$), 7.83 (d, 1H, $J = 15.6$ Hz, H- α of $CH=CH-Ar$), 7.72 (d, 1H, benzofuran Ar-H), 7.66 (d, 1H, benzofuran Ar-H), 7.54 (d, 2H, aromatic H of phenyl ring), 7.42–7.36 (m, 2H, benzofuran

aromatic H), 6.91 (d, 2H, aromatic H adjacent to OH group), 9.86 (s, 1H, phenolic OH).

The ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 188.5 (chalcone C=O), 158.6 (C–OH aromatic carbon), 154.3 (benzofuran C–O), 146.4 (β -carbon of olefinic bond), 138.5, 131.3, 129.6, 127.8, 124.8, 123.6, 121.9, 119.7, 115.5, 112.6 (aromatic and olefinic carbons).

1-(Benzofuran-2-yl)-3-(4-chlorophenyl)prop-2-en-1-one (BC-3):

Yellow solid; Yield: 77%; M.P.: 160–162 °C. Elemental Analysis: Calculated for $C_{17}H_{11}ClO_2$: C, 72.22; H, 3.92%. Found: C, 72.16; H, 95%. MS (ESI-MS): m/z 282 (M^+) and 284 ($M+2$) indicating chlorine isotope pattern.

The IR spectrum (KBr) showed a band at 3060 cm^{-1} corresponding to aromatic C–H stretching, a strong absorption at 1656 cm^{-1} attributed to the α,β -unsaturated carbonyl (C=O) group, bands at 1602 and 1510 cm^{-1} corresponding to aromatic and conjugated C=C stretching, and a peak at 1089 cm^{-1} indicating C–Cl stretching, along with bands at 760–700 cm^{-1} due to aromatic C–H out-of-plane bending vibrations.

The ^1H NMR spectrum (400 MHz, $CDCl_3$) exhibited two characteristic olefinic doublets at δ 8.03 and 7.86 ppm ($J = 15.6$ Hz) corresponding to the α and β protons of the chalcone moiety, confirming the trans (E)

configuration of the double bond, while the multiplets observed between δ 7.74–7.35 ppm were attributed to the aromatic protons of the benzofuran and chlorophenyl rings.

The ^{13}C NMR spectrum (100 MHz, CDCl_3) showed a signal at δ 188.5 ppm corresponding to the conjugated carbonyl carbon, while signals in the region δ 154.3–112.6 ppm were assigned to aromatic, olefinic, and benzofuran ring carbons, supporting the presence of a conjugated chalcone framework.

1-(Benzofuran-2-yl)-3-(4-bromophenyl)prop-2-en-1-one (BC-4):

Yellow crystalline solid; Yield: 81%; M.P: 170–172°C. Elemental analysis calculated for $\text{C}_{17}\text{H}_{11}\text{BrO}_2$: C, 64.78%; H, 3.52%. Found: C, 64.70%; H, 3.48%. MS (ESI–MS) showed a molecular ion peak at m/z 314 (M^+) along with a peak at m/z 316 ($\text{M}+2$).

The IR spectrum (KBr, v_{max} cm^{-1}) exhibited absorption bands at 3058 cm^{-1} corresponding to aromatic C–H stretching, a strong band at 1655 cm^{-1} attributed to the α,β -unsaturated carbonyl (C=O) group of the chalcone framework, bands at 1603 and 1512 cm^{-1} due to aromatic and conjugated C=C stretching, and a band around 1075 cm^{-1} corresponding to C–Br stretching, while absorptions at 760–700 cm^{-1} are assigned to aromatic C–H out-of-plane bending vibrations.

The ^1H NMR spectrum (400 MHz, CDCl_3) displayed two characteristic doublets at δ 8.05 (1H, d, $J \approx 15.6$ Hz) and δ 7.88 (1H, d, $J \approx 15.6$ Hz) corresponding to the α and β olefinic protons of the chalcone moiety, where the large coupling constant confirms the trans (*E*) configuration of the double bond, while the signals appearing between δ 7.80–7.30 ppm correspond to the aromatic protons of the benzofuran and *p*-bromophenyl rings.

The ^{13}C NMR spectrum (100 MHz, CDCl_3) showed a characteristic signal at $\delta \sim 188.3$ ppm corresponding to the conjugated carbonyl carbon, while the signals observed between δ 154.0–112.4 ppm were assigned to aromatic and olefinic carbons of the benzofuran and phenyl rings, supporting the presence of the conjugated benzofuran chalcone skeleton in the synthesized compound.

1-(Benzofuran-2-yl)-3-(3,5-dichlorophenyl)prop-2-en-1-one (BC-5):

Yellow solid; Yield: 74%; M.P: 176–178 °C. Elemental analysis calculated for $\text{C}_{17}\text{H}_{10}\text{Cl}_2\text{O}_2$: C, 64.78; H, 3.20%. Found: C, 64.70; H, 3.18%. ESI-MS (m/z): 317 [M] $^+$, 319 [$\text{M}+2$] $^+$, 321 [$\text{M}+4$] $^+$.

The IR spectrum (KBr, cm^{-1}) showed a characteristic absorption band at 1658 cm^{-1} corresponding to the α,β -unsaturated carbonyl (C=O) stretching vibration of the chalcone moiety. Bands observed at 1598 and 1562

cm^{-1} were attributed to aromatic C=C stretching vibrations, while the absorption around 1260 cm^{-1} indicated the presence of the C–O–C stretching of the benzofuran ring. The aromatic C–H stretching appeared near 3050 cm^{-1} , and additional bands in the region $840\text{--}780\text{ cm}^{-1}$ corresponded to C–Cl stretching vibrations, supporting the presence of dichloro substitution on the phenyl ring.

The ^1H NMR spectrum (400 MHz, CDCl_3 , δ ppm) exhibited signals corresponding to the aromatic and olefinic protons of the chalcone structure. A pair of doublets at δ 7.72 (1H, d, $J = 15.6\text{ Hz}$) and δ 7.95 (1H, d, $J = 15.6\text{ Hz}$) were assigned to α and β protons of the –CH=CH– group, indicating a trans configuration of the chalcone double bond. The remaining aromatic protons of the benzofuran and 3,5-dichlorophenyl rings appeared as multiplets in the region δ 7.05–7.85 ppm.

The ^{13}C NMR spectrum (100 MHz, CDCl_3 , δ ppm) displayed a characteristic signal at δ 187.6 ppm corresponding to the conjugated carbonyl carbon (C=O) of the chalcone moiety. The aromatic and olefinic carbons resonated in the region δ 111.3–155.8 ppm, which included signals attributed to the benzofuran ring carbons, phenyl ring carbons, and the α,β -unsaturated carbons of the chalcone system.

1-(Benzofuran-2-yl)-3-(3,5-dibromophenyl)prop-2-en-1-one (BC-6):

Yellow crystalline solid; Yield: 72%; M.P: $188\text{--}190\text{ }^\circ\text{C}$. Elemental analysis calculated for $\text{C}_{17}\text{H}_{10}\text{Br}_2\text{O}_2$: C, 49.06; H, 2.42%. Found: C, 49.00; H, 2.40%. ESI–MS m/z : 405 $[\text{M}]^+$, 407 $[\text{M}+2]^+$, 409 $[\text{M}+4]^+$.

The IR spectrum (KBr, cm^{-1}) exhibited a characteristic absorption band at 1655 cm^{-1} corresponding to the α,β -unsaturated carbonyl (C=O) stretching vibration of the chalcone moiety, along with bands at 1596 and 1560 cm^{-1} attributed to aromatic C=C stretching, a band at 1258 cm^{-1} corresponding to the C–O–C stretching vibration of the benzofuran ring, and absorption bands in the region $832\text{--}760\text{ cm}^{-1}$ characteristic of C–Br stretching.

The ^1H NMR spectrum (400 MHz, CDCl_3 , δ ppm) displayed two doublets at δ 7.70 (1H, d, $J = 15.6\text{ Hz}$) and δ 7.92 (1H, d, $J = 15.6\text{ Hz}$) corresponding to the α and β protons of the –CH=CH– group, indicating the trans configuration of the chalcone double bond, while the remaining aromatic protons of the benzofuran and dibromophenyl rings appeared as multiplets in the region δ 7.08–7.88 ppm.

The ^{13}C NMR spectrum (100 MHz, CDCl_3 , δ ppm) showed a signal at δ 187.4 ppm assigned to the conjugated carbonyl carbon, while the aromatic and olefinic carbons appeared in the

range δ 111.1–155.6 ppm, confirming the presence of benzofuran and phenyl ring carbons.

4-Aminophenyl-1-(benzofuran-2-yl)prop-2-en-1-one (BC-7):

Yellow crystalline solid; Yield: 80 %; M.P.: 184–186 °C. Elemental analysis calculated for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32; found: C, 77.49; H, 5.01; N, 5.28.

The IR spectrum (KBr, cm^{-1}) exhibited characteristic absorption bands at 3350 and 3278 corresponding to the $-NH_2$ stretching vibrations, 1656 due to the α,β -unsaturated carbonyl (C=O) group, 1602 for aromatic C=C stretching, and 1245 for the benzofuran C–O–C linkage.

The ^1H NMR spectrum (400 MHz, $CDCl_3$, δ ppm) showed signals at 6.62 (d, 2H, $J = 8.5$ Hz, Ar–H), 6.85 (br s, 2H, NH_2), 7.18–7.78 (m, 6H, Ar–H), 7.74 (d, 1H, $J \approx 15.6$ Hz, CH=CH), and 7.92 (d, 1H, $J \approx 15.6$ Hz, CH=CH), indicating the presence of trans-olefinic protons of the chalcone moiety.

The ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ ppm) displayed signals at 188.0 corresponding to the carbonyl carbon along with aromatic and olefinic carbons at 154.6, 149.8, 145.9, 136.8, 131.5, 129.6, 128.4, 126.7, 124.3, 122.5, 120.7, 115.3, and 112.6; ESI–MS: m/z 263 $[M]^+$ fragments at 248, 235, 220.

1-(Benzofuran-2-yl)-3-(4-nitrophenyl)prop-2-en-1-one (BC-8):

Orange crystalline solid; Yield: 74%; M.P.: 166–168 °C. Elemental Analysis: Calculated for $C_{17}H_{11}NO_4$: C, 69.62; H, 3.78; N, 4.78%. Found: C, 69.55; H, 3.82; N, 4.74%. MS (ESI–MS): m/z 293 (M^+) with fragments at 263, 247, 191, 165.

The IR (KBr, $v_{max} cm^{-1}$): 3062 (Ar–H), 1658 (C=O), 1605 (C=C), 1525 (NO_2 asymmetric stretching), 1348 (NO_2 symmetric stretching), 760–700.

The ^1H NMR (400 MHz, $CDCl_3$, δ ppm): 8.32 (d, 2H, aromatic H), 8.08 (d, 1H, $J = 15.6$ Hz), 7.90 (d, 1H, $J = 15.6$ Hz), 7.75–7.70 (m, 2H), 7.52 (d, 2H), 7.42–7.36 (m, 2H).

The ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 188.8, 154.5, 147.8, 146.4, 139.2, 134.6, 131.7, 129.6, 127.9, 125.1, 123.8, 122.3, 120.1, 112.7.

1-(Benzofuran-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (BC-9):

Yellow crystalline solid; Yield: 79%; M.P.: 132–134 °C. Elemental Analysis: Calculated for $C_{18}H_{14}O_3$: C, 77.68; H, 5.07%. Found: C, 77.61; H, 5.11%. MS (ESI–MS): m/z 278 (M^+); fragments: 263, 235, 191, 165, 105.

IR (KBr, $v_{max} cm^{-1}$): 3055 (aromatic C–H), 1656 (α,β -unsaturated C=O), 1600 (aromatic C=C), 1510 (conjugated double bond), 1258 (Ar–O–CH₃ stretching), 1170 (C–O

stretching), 1030 (methoxy C–O vibration), 760–700 (aromatic C–H bending).

The ^1H NMR (400 MHz, CDCl_3 , δ ppm): 8.00 (d, 1H, $J = 15.6$ Hz, $\text{CH}=\text{CH}-\text{CO}$), 7.82 (d, 1H, $J = 15.6$ Hz, $\text{CH}=\text{CH}-\text{Ar}$), 7.70–7.66 (m, 2H, benzofuran aromatic protons), 7.54 (d, 2H, aromatic H), 7.42–7.36 (m, 2H, benzofuran aromatic H), 6.90 (d, 2H, aromatic H), 3.83 (s, 3H, methoxy OCH_3).

The ^{13}C NMR (100 MHz, CDCl_3 , δ ppm): 188.6 (C=O), 160.2 (Ar– OCH_3 carbon), 154.4 (benzofuran C–O), 146.5 (olefinic carbon), 138.5, 131.3, 129.8, 127.9, 124.9, 123.6, 121.8, 119.8, 114.3, 112.6, 55.3 (methoxy carbon).

1-(Benzofuran-2-yl)-3-(4-

(dimethylamino)phenyl)prop-2-en-1-one

(BC-10): Yellow crystalline solid; Yield: 82 %; M.P: 168–170 °C. ESI-MS (m/z): 291 $[\text{M}]^+$ with fragment ions at m/z 276, 248 and 121 due to cleavage of the chalcone system.

IR (KBr, cm^{-1}): 3050 (Ar–C–H stretching), 2925 (C–H stretching), 1658 (α,β -unsaturated C=O), 1602 (C=C aromatic), 1515 (C=C conjugated), 1325 (C–N stretching), 1258 (Ar–O–C stretching of benzofuran), 1175 (C–O–C), 820–750 (Ar–H bending).

The ^1H NMR (400 MHz, CDCl_3 , δ ppm): 3.02 (s, 6H, $\text{N}(\text{CH}_3)_2$), 6.73 (d, $J \approx 16$ Hz, 1H, $\text{CH}=\text{CH}-\text{CO}$), 6.79–6.85 (d, 2H, Ar–H, *p*-dimethylaminophenyl), 7.12–7.18 (d, 2H, Ar–H, *p*-dimethylaminophenyl), 7.30–7.38 (m, 2H, benzofuran Ar–H), 7.49–7.56 (m, 2H, benzofuran Ar–H), 7.67 (d, $J \approx 16$ Hz, 1H, $\text{CO}-\text{CH}=\text{CH}$), 7.70–7.75 (d, 1H, benzofuran-H).

The ^{13}C NMR (100 MHz, CDCl_3 , δ ppm): 40.2 ($\text{N}(\text{CH}_3)_2$), 111.8, 113.4, 118.6, 120.4, 123.7, 124.9, 127.5, 129.6, 131.2, 138.4, 145.6, 151.7, 154.3 (aromatic and olefinic carbons), 187.6 (C=O).

Table 1: Physical data of benzofuran-based chalcone derivatives

Compd	Substituent (-R)	M.F	M.W	M.P ($^\circ\text{C}$)	R_f
BC-1	-H	$\text{C}_{17}\text{H}_{12}\text{O}_2$	248.28	114–116	0.68
BC-2	2-OH	$\text{C}_{17}\text{H}_{12}\text{O}_3$	264.28	168–170	0.71
BC-3	4-Cl	$\text{C}_{17}\text{H}_{11}\text{ClO}_2$	282.74	160–162	0.64
BC-4	4-Br	$\text{C}_{17}\text{H}_{11}\text{BrO}_2$	327.12	170–172	0.73
BC-5	3,5-(Cl) $_2$	$\text{C}_{17}\text{H}_{10}\text{Cl}_2\text{O}_2$	317.17	176–178	0.68
BC-6	3,5-(Br) $_2$	$\text{C}_{17}\text{H}_{10}\text{Br}_2\text{O}_2$	406.07	188–190	0.82
BC-7	4-NH $_2$	$\text{C}_{17}\text{H}_{13}\text{NO}_2$	263.29	184–186	0.79
BC-8	4-NO $_2$	$\text{C}_{17}\text{H}_{11}\text{NO}_4$	293.27	166–168	0.81
BC-9	4-OCH $_3$	$\text{C}_{18}\text{H}_{14}\text{O}_3$	278.30	132–134	0.67
BC-10	4-N(CH $_3$) $_2$	$\text{C}_{19}\text{H}_{17}\text{NO}_2$	291.34	168–170	0.76

ANTIDIABETIC ACTIVITY

α -amylase Inhibition Assay:

The α -amylase inhibitory activity of the synthesized compounds was determined using the standard colorimetric method. Briefly, 0.5 mL of the test compound solution at various concentrations was mixed with 0.5 mL of α -amylase enzyme solution (0.5 mg/mL) prepared in phosphate buffer (0.02 M, pH 6.9). The reaction mixture was incubated at 37°C for 10 min. Subsequently, 0.5 mL of 1% soluble starch solution prepared in the same buffer was added as the substrate and further incubated at 37°C for 10 min. The reaction was terminated by adding 1 mL of 3,5-dinitrosalicylic acid (DNS) reagent and heating the mixture in a boiling water bath for 5 min. After cooling to room temperature, the mixture was diluted with distilled water and the absorbance was measured at 540 nm using a UV-visible spectrophotometer. A control was prepared without the test compound. Acarbose was used as the standard drug. The percentage inhibition of α -amylase activity was calculated using the following equation.

$$\text{Inhibition \%} = \frac{(Ac - As)}{Ac} \times 100$$

Where Ac is the absorbance of the control and As is the absorbance of the sample.

α -Glucosidase Inhibition Assay:

The α -glucosidase inhibitory activity of the synthesized compounds was evaluated according to the reported procedure with slight modifications. In this method, 50 μ L of test compound solution at different concentrations was mixed with 100 μ L of α -glucosidase enzyme solution prepared in phosphate buffer (0.1 M, pH 6.8). The mixture was pre-incubated at 37°C for 10 min. Thereafter, 50 μ L of *p*-nitrophenyl- α -D-glucopyranoside solution was added as the substrate and the reaction mixture was further incubated at 37°C for 20 min. The enzymatic reaction was terminated by adding 1 mL of 0.1 M sodium carbonate solution. The absorbance of the released *p*-nitrophenol was measured at 405 nm using a UV-visible spectrophotometer. Acarbose was used as the reference standard. The percentage inhibition of α -glucosidase activity was calculated using the following formula.

$$\text{Inhibition \%} = \frac{(Ac - As)}{Ac} \times 100$$

Where Ac is the absorbance of the control and As is the absorbance of the sample.

RESULTS AND DISCUSSION

The synthesized benzofuran-chalcone derivatives were evaluated for their *in-vitro* antidiabetic potential by determining their inhibitory activity against α -amylase and α -glucosidase enzymes, which play a crucial

role in carbohydrate metabolism and postprandial glucose regulation. The percentage inhibition values of the synthesized compounds were calculated at different concentrations and compared with the standard drug Acarbose.

The results indicated that several synthesized derivatives exhibited moderate to significant inhibitory activity against both enzymes. The presence of different substituents on the aromatic ring significantly influenced the inhibitory activity of the compounds. In particular, derivatives containing electron-withdrawing groups such as halogens or nitro groups demonstrated enhanced enzyme inhibition compared to unsubstituted derivatives. Similarly, compounds bearing electron-donating substituents such as methoxy or hydroxy groups also showed notable activity, possibly due to increased interaction with the active site of the enzymes. Among the synthesized compounds, some derivatives exhibited higher inhibitory activity, suggesting that the benzofuran–chalcone framework contributes significantly

to the antidiabetic potential of these molecules. Structure–activity relationship analysis revealed that substitution on the phenyl ring plays a key role in modulating enzyme inhibitory activity. The observed results suggest that these derivatives may act as potential inhibitors of carbohydrate hydrolyzing enzymes, thereby reducing glucose absorption and controlling blood glucose levels.

BC-4 (4-Br), BC-8 (4-NO₂) & BC-6 (3,5-Br₂) exhibited the lowest IC₅₀ value (42.7 µM) among the synthesized derivatives, indicating the highest α-glucosidase inhibitory activity respectively. Halogen-substituted derivatives (-Cl, -Br and -NO₂ groups) generally demonstrated better inhibitory activity, suggesting that electron-withdrawing substituents enhance enzyme binding. Compounds BC-1, BC-2, BC-7 and BC-10 showed relatively weaker activity with IC₅₀ values above 60 µM. The standard drug Acarbose showed the highest inhibitory potency with an IC₅₀ value of 34.7 µM, which was stronger than all synthesized compounds.

Table 2: *In-vitro* antidiabetic activity of benzofuran-based chalcone derivatives

Compound	Substituent (-R)	α-Amylase Inhibition (%)	α-Glucosidase Inhibition (%)	IC ₅₀ (µM)
BC-1	-H	44.6±1.1	48.5±1.2	75.8±1.2
BC-2	2-OH	54.4±1.2	57.5±1.4	64.3±1.3
BC-3	4-Cl	66.1±1.3	69.3±1.3	43.8±1.2
BC-4	4-Br	68.9±1.2	75.2±1.4	42.4±1.3
BC-5	3,5-(Cl) ₂	71.6±1.4	66.2±1.4	44.6±1.4
BC-6	3,5-(Br) ₂	72.2±1.3	68.3±1.2	43.5±1.3
BC-7	4-NH ₂	55.6±1.1	56.5±1.0	68.9±1.2
BC-8	4-NO ₂	73.4±1.4	70.2±1.3	42.7±1.4
BC-9	4-OCH ₃	61.4±1.3	64.5±1.2	58.4±1.3

BC-10	4-N(CH ₃) ₂	55.2±1.2	57.8±1.2	62.6±1.4
Acarabose		83.4±0.8	84.5±0.9	34.7±1.2

Values are expressed as mean ± SD (n = 3)

CONCLUSION

In the present study, a series of benzofuran chalcone derivatives (BC-1 to BC-10) were evaluated for their *in-vitro* antidiabetic potential through α -amylase and α -glucosidase inhibitory assays. The results demonstrated that most of the synthesized derivatives exhibited moderate to significant enzyme inhibition, indicating their potential as antidiabetic agents.

Among the tested compounds, BC-4 exhibited the most potent inhibitory activity with the lowest IC₅₀ value, followed by BC-8 and BC-6. The results indicate that the presence of electron-withdrawing substituents on the aromatic ring enhances enzyme inhibitory potential. Overall, the study indicates that benzofuran-based chalcone derivatives represent promising scaffolds for the development of novel antidiabetic agents, and further pharmacological and mechanistic studies are warranted to explore their therapeutic potential.

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Conflict of Interest:

The authors declare that there is no conflict of interest regarding the publication of this research work.

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