Original Article

Absence of antidiabetic activity in some novel thiazolidinone derivatives

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Abstract

Aim: It was aimed to synthesise some novel thiazolidinone derivatives and assess them for antidiabetic activity. **Material and Methods:** A series of substituted 5-ethylidene-2-(phenylimino) thiazolidin-4-ones were prepared by using phenylthiourea (I) as a starting material. Phenylthiourea on reaction with ethylchloroacetate, in the presence of ethanol and fused sodium acetate, gave 2-(phenylimino) thiazolidin-4-one (II), and 2-(phenylimino) thiazolidin-4-one on further reaction with substituted benzaldehyde gave substituted 5-ethylidene-2- (phenylimino) thiazolidin-4-one (III – XVIII). The synthesized compounds were authenticated on the basis of elemental analysis, IR, 1H NMR, and Mass spectral analysis and some of the compounds were selected on the basis of a literature review, to evaluate them for their antidiabetic activity. **Results and Conclusion:** All The tested compounds 5-(4-fluorobenzylidene)-2-(phenylimino) thiazolidin-4-on (VII) and 5-(4-Methylbenzylidene)-2-(phenylimino)thiazolidin-4-one (X), 5-(2, 4-dinitrobenzylidene)-2-(phenylamino) thiazolidin-4-one (XVII) were found to be ineffective in lowering the blood glucose level.

Key words: Heterocyclic, substitution, synthesis, thiazole, thiazolidinone

INTRODUCTION

Diabetes belongs to a group of metabolic disorders in which the body is not able to produce sufficient amount of insulin or the body cells do not respond to the insulin that is produced, leading to symptoms such as increased urination, extreme thirst, and unexplained weight loss. In its most severe form, ketoacidosis or a non-kenotic hyperosmolar state may develop and lead to stupor, coma, and in absence of effective treatment, often death.[1] Insulin is the principal hormone that regulates the uptake of glucose from the blood into most cells (primarily muscle and fat cells, but not central the nervous system cells). Therefore, deficiency of insulin or the insensitivity of its receptors plays a central role in all forms of diabetes mellitus.[2] Diabetes is mainly divided into three types Type I or Insulin-dependent diabetes mellitus (IDDM), which includes those cases that occur due to an autoimmune process, as well as those with beta-cell destruction, and in those who are prone to ketoacidosis for which neither an etiology nor a pathogenesis is known (idiopathic). It does not include those forms of beta-cell destruction or failure to which specific causes can be assigned (e.g. cystic fibrosis, mitochondrial defects, and the like). Type II or non-insulin dependent diabetes mellitus (NIDDM) includes the common form of diabetes, which results from a defect in insulin secretion, almost with a major contribution from insulin resistance.[3] Type III gestational diabetes is a hyperglycemic condition that occurs due to carbohydrate intolerance, with onset or first recognition during pregnancy. The definition applies irrespective of whether or not insulin is used for treatment or the condition persists after pregnancy. Individuals at high risk for gestational diabetes include

Access this article online

Quick Response Code:

Website: www.pnrjournal.com

DOI: 10.4103/0976-9234.116768

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older women, those with a previous history of glucose intolerance. As far as the antidiabetic activity is concerned thiazolidinone has been reported to possess diversified activities including hypoglycemic action.[4] Drugs like Pioglitazone and Rosiglitazone contain a heterocyclic thiazolidinone ring, which plays an important role in antidiabetic activity.[5]

Chemistry

The chemistry of a thiazolidin-4-one ring system is of considerable interest as it is the core structure in various synthetic pharmaceuticals, which display a broad spectrum of biological activities. These are heterocyclic compounds that have an atom of sulfur at position 1, an atom of nitrogen at position 3, and a carbonyl group at position 4.[6] Heterocyclic compounds are cyclic compounds with at least two different elements as ring member atoms.[7] They are the counter parts of homocyclic compounds, which have ring atoms from the same element. Although heterocyclic compounds may be inorganic, most of them contain at least one carbon atom, and one or more atoms of elements other than carbon within the ring structure, such as sulfur, oxygen or nitrogen.[8] Thiazolidinone, a saturated form of thiazole, with a carbonyl group on the fourth carbon, has been considered to have a large number of biological activities [Figure 1].

Substitution can be done at positions 2, 3, and 5, but the greatest difference in structure and properties is exerted by the group attached to the carbon atom in position 2 [Figure 2]. The carbonyl group present in the moiety is highly unreactive. The tetrahydro derivative of thiazole is known as thiazolidine and the oxo-derivative of thiazolidine is known as thiazolidinone.

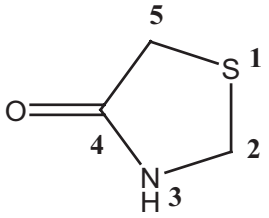
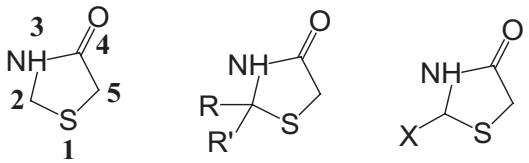


Figure 1: Structure of 4-Thiazolidinone



X = [= O, = S, NR, NN = CRR']
R, R' = Cl, F, C_5H_5Cl

Figure 2: Various Thiazolidinone rings and their substituents

The 3-unsubstituted thiazolidinones are usually solids, but the attachment of an alkyl group to the nitrogen lowers the melting point. The thiazolidinones that do not contain aryl or higher alkyl substituents are slightly soluble in water.[9] 4-Thiazolidinone derivatives are known to possess antibacterial,[10,11] antifungal,[12,13] antiviral,[14,15] antituberculosis,[16] and anti-convulsant[17] properties. 4-Thiazolidinones have been reported as novel inhibitors of the bacterial enzyme Mur B, which is a precursor, which acts during the biosynthesis of peptidoglycan.[18] 4-Thiazolidinones of diflunisal have been found to be dual acting antimicrobial / antituberculosis agents possessing anti-inflammatory properties via the active metabolite, diflunisal, and are active against pain and inflammatory events, due to the cell damage arising from tuberculosis and the accompanying infectious diseases.[19] 2, 3-disubstituted analogs of Thiazolidinone have proved to be predominantly effective non-nucleoside HIV reverse-transcriptase inhibitors.[20] It was observed that reaction with cyclizing reagents like α-halocarbonyl compounds such as, $ClCH_2COCl$, $BrCH_2COCl$, $BrCH_2COOEt$, and $ClCH_2COCH_2COOEt$ in boiling ethanol, with fused sodium acetate, have better biological profiles and a better yield.[21,22] The thiazolidin-4-one ring system also occurs in nature as asactithiazic acid, ((-)2-(5-carboxypentyl)thiazolidin-4-one), which is isolated from the *Streptomyces* strains.[22]

MATERIALS AND METHODS

All the chemicals and reagents were obtained from Sigma (Germany) and CDH (India) and were recrystallized / redistilled as necessary. The melting points were determined by the open capillary tube method. The purity of the compounds was checked on thin layer chromatography (TLC) plates, which were precoated with silica gel G using solvent system toluene : ethyl acetate : formic acid (5 : 4 : 1). The spots were located under iodine vapors and ultraviolet (UV) light. Infrared (IR) spectra were recorded using KBr on Fourier transform infrared (FTIR) Shimadzu 8400S IR spectrophotometer (Japan). A JEOL AL300 FTNMR 300 MHz spectrometer was used to acquire High Resolution Nuclear Magnetic Resonance (^{1}HNMR) spectra with Acetone as the solvent and tetramethylsilane (TMS) as the internal standard. Chemical shift values are expressed in ppm. Mass spectra were obtained using a Kratos-AEI MS-902S instrument. Elemental analyses were carried out with a Perkin Elmer Model 240-C apparatus (CDRI,

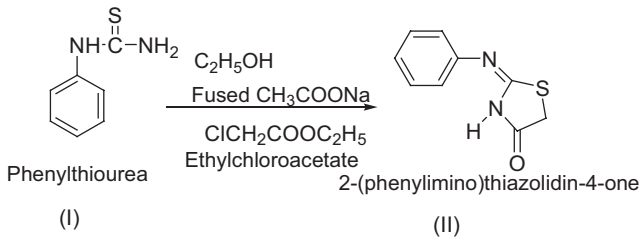
Lucknow). The results of the elemental analysis (C, N, and S) were within ± 0.4% of the calculated amounts.

Synthesis

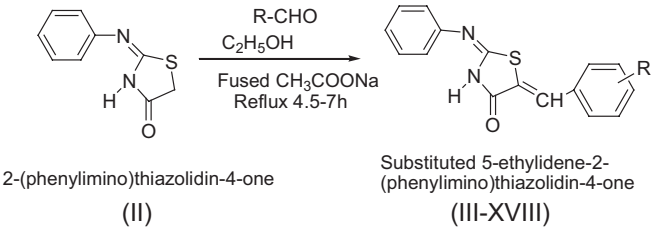
Step 1

General Procedure for synthesis of 2-phenyliminothiazolidin-4-one (II)

Phenyl thiourea **(I)** 8 g (0.04 moles) was dissolved in 16.45 ml ethanol. The resulting mixture was refluxed with fused sodium acetate 4.31g (0.052 moles) and ethylchloroacetate 6.46 g (5.65 ml) for four hours. The reaction mixture was then poured into water. The reaction mixture was kept overnight for complete precipitation. The precipitate obtained was filtered and dried at room temperature. Further it was recrystallized with ethanol [Scheme 1].



Scheme 1: Synthesis of 2-(phenylimino) thiazolidin-4-one



Scheme 2: Synthesis of substituted 5-ethylidene-2-(phenylimino) thiazolidin-4-ones

2-phenyliminothiazolidin-4-one (II)

Yield: 80.79% (solid); m.p: 175–177°C; R_f value (T: E: F; 5: 4: 1): 0.75, IR (KBr): 3415(N-H), 1745(C = O), 1610 (C = N)cm^{-1}, ^{1}H NMR (Acetoned-6, 300 MHz): δ = 3.21 (s, 2H, CH_2), 6.98 – 7.34 (m, 5 H, phenyl), 11.82 (s, 1H, NH), MS m / z: 192 (M^+), Anal. Calcd for $C_9H_8N_2OS$: C, 55.26; N, 14.10; S, 16.60 [Table 1].

Step-2

2.2.2 General Procedure for the preparation of substituted Thiazolidinone Derivatives (III–XVIII)

2-phenyliminothiazolidin-4-one (II) (0.01 mole) was reacted with different aromatic aldehydes (0.01 mole) with fused sodium acetate (0.01mole) in ethanol (8 ml) for six to seven hours. The reaction mixture was then cooled to room temperature, poured into ice cold water and kept overnight. The precipitate obtained was filtered and washed with water to remove the aldehyde that had not reacted. Further this precipitate was dried at room temperature. The product obtained was recrystallized from dimethyl formamide [Scheme II].

Table 1: Physical property of synthesized compound (II)

Compound	R	Molecular formula	M. Wt	Rf Value	%Yield
II	H	C9H8N20S	192.24	0.75	80.79

Solvent system used: Toluene : Ethyl acetate : Formic acid (5:4:1)

Table 2: Physical properties of synthesized compounds (III–XVIII)

Compound code	R	Molecular Formula	Mol. Wt.	m.p.(°C)	Yield (%)	R^f
III	Benzaldehyde	$C_6H_{12}N_2OS$	280.34	258 – 260	68.80	0.71
IV	2,4dichlorobenzaldehyde	$C_{16}H_{10}C_{l2}N_2S$	349.23	186 – 188	87.90	0.67
V	2-Nitrobenzaldehyde	$C_{16}H_{11}N_3O_3S$	325.34	297 – 299	41.20	0.76
VI	4-Methoxybenzaldehyde	$C_{17}H_{14}N_2O_2S$	310.37	195 – 197	93.75	0.63
VII	4-Fluorobenzaldehyde	$C_{16}H_{11}FN_2OS$	298.33	272 – 274	66.00	0.68
VIII	3,4,5trimethoxybenzaldehyde	$C_{19}H_{18}N_2O_4S$	370.42	210 – 212	62.16	0.70
IX	4-chlorobenzaldehyde	$C_{16}H_{11}ClN_2OS$	314.79	285 – 287	76.19	0.80
X	4-Methylbenzaldehyde	$C_{17}H_{14}N_2OS$	294.37	202 – 204	62.00	0.72
XI	5-Methylsalicyldehyde	$C_{17}H_{14}N_2O_2S$	310.37	239 – 241	71.10	0.77
XII	4-Nitrobenzaldehyde	$C_{16}H_{11}N_3O_3S$	325.34	320 – 322	54.50	0.73
XIII	2-chlorobenzaldehyde	$C_{16}H_{11}ClN_2OS$	314.79	200 – 202	82.80	0.65
XIV	Anisaldehyde	$C_{16}H_{12}N_2O_2S$	296.34	280 – 282	61.00	0.78
XV	2,4difluorobenzaldehyde	$C_{16}H_{10}F_2N_2OS$	316.33	240 – 242	60.50	0.62
XIV	2-Fluorobenzaldehyde	$C_{16}H_{11}FN_2OS$	298.33	260 – 262	82.20	0.76
XVII	2,4dinitrobenzaldehyde	C\H\N$_4$O$_5$S	370.34	242 – 244	51.40	0.74
XVIII	2-Bromobenzaldehyde	$C_{16}H_{11}BrN_2OS$	359.24	270 – 272	78.20	0.60

TLC Solvent system used: Toluene: Ethyl acetate: Formic acid (5:4:1)

Spectral data of compounds

5-Benzyliden-2-(phenylimino) thiazolidin-4-ones (III)

Yield: 68.80% (solid); m.p: 258–260°C, Rf value (T: E: F; 5:4:1): 0.71, IR (KBr) cm-1: 3251.76 (N-H); 30251.76 (Ar C-H); 1677.95 (C = O); 1637.45 (C = N). 1H NMR (Acetone-d6, 300 MHz, δ ppm); 6.9 – 7.8 (m, 10H, phenyl and benzylidene); 7.35 (s, 1H, C = CH); 7.8 (s, 1H, NH), Mass (m / z) 495.0 (M+). Anal. Calcd (C6H12N2OS): C, 67.20; N, 8.90; S, 11.40.

5-(2, 4-dichlorobenzylidene)-2-(phenylimino) thiazolidin-4-one (IV)

Yield 87.90% (solid); mp 186 – 188°C, R_f value (T: E: F; 5: 4: 1): 0.67, IR (KBr) cm^{-1}: 3461.47 (N-H); 3037.21 (Ar C-H), 2953.56 (aliphatic C-H), 1671.62 (C = O), ^{1}H NMR (Acetone-d6,300 MHz, δ ppm) 6.99 – 7.20 (m,10H, phenyl and benzylidene); 7.60 (s,1H,C = CH); 8.2 (s, 1H, NH), Mass (m / z) 347.98 (M^+). Anal. Calcd ($C_{16}H_{10}C_{l2}N_2OS$): C, 55.0; N, 8.00; S, 9.10 [Table 2].

5-(2-nitrobenzylidene)-2-(phenylimino) thiazolidin-4-one (V)

Yield: 41.20% (solid); m.p: 297-300°C, R_f value (T: E: F; 5:4:1): 0.76, IR (KBr) cm^{-1}: 3420 (N-H); 3031 (Ar C-H); 1660 (C = O); 1600 (C = N); 1492 (C-NO_2); ^{1}H NMR (Acetone-d6,300 MHz, δ ppm): 6.90 – 7.32 (m, 5H,phenyl); 7.60 (s,1H,C = CH); 7.70-8.24 (m, 4H, 3-nitrobenzylidene); 8.7 (s, 1H, NH), Mass (m / z) 325.04 (M^+). Anal. Calcd $C_{16}H_{11}N_3O_3S$: C, 59.06; N, 12.90; S, 9.82 [Table 2].

5-(4-methoxybenzylidene)-2-(phenylamino) thiazolidin-4-one (VI)

Yield: 93.75% (solid); m.p: 195-197°C, R_f value (T: E: F; 5:4:1): 0.63, IR (KBr) cm^{-1}: 1674.10 (C = 0), 1384.79 (CH = CH), 1244.00 (N-H), ^{1}H NMR (Acetone-d6, 300 MHz, δ ppm): 7.34 – 7.60 (m, 9H, phenyl and benzylidene); 7.39 (m, 1H, C = CH); 7.8 (s, 1H, NH), Mass (m / z) 386.1 (M^+). Anal. Calcd ($C_{17}H_{14}N_2O_2S$): Calcd C 65.30, N 8.97, S, 10.25 [Table 2].

5-(4-fluorobenzylidene)-2-(phenylimino) thiazolidin-4-on (VII)

Yield: 66.00%(solid); m.p: 272 – 274°C, R_f value(T: E: F; 5:4:1): 0.68, IR (KBr) cm^{-1}: 3467 (N-H); 3050 (Ar C-H); 1680 (C = 0); 1600 (C = N);1032 (C-F); ^{1}H NMR (Acetone-d6, 300 MHz, δ ppm): 6.89–7.34 (m, 5H, phenyl); 7.13 (d, 2H, benzylidine); 6.91 (d, 2H, benzylidine), 7.39 (s, 1H,C = CH); 7.73 (s, 1H, NH), Mass (m / z) 374.1 (M^+). Anal. Calcd ($C_{16}H_{11}FN_2OS$): C, 64.40; N, 9.35; S, 10.73 [Table 2].

5-(3, 4, 5-trimethoxybenzylidene)-2-(phenylimino) thiazolidin-4-one (VIII)

Yield: 62.16% (solid); m.p: 210–212°C, R_f value (T: E: F; 5: 4: 1): 0.70; IR (KBr) cm^{-1}: 1660.23 (C = O), 1180.86 (CH = CH), 1220.24 (CH = CH), ^{1}H NMR (Acetone-d6, 300 MHz, δ ppm): 3.82 (s, 9H, OCH_3); 8.14 (s, 1H, C = CH); 8.01 (s, 1H, NH) Mass (m / z) 390.09 (M^+). Anal. Calcd ($C_{19}H_{18}N_2O_4S$): C, 61.61; N, 7.54; S, 8.60 [Table 2].

5-(4-chlorobenzylidene)-2-(phenylimino) thiazolidin-4-one (IX)

Yield: 76.19%, m.p: 285–287°C; R_f value (T: E: F; 5: 4: 1): 0.80; IR (KBr) cm^{-1}: 1633.59 (C = O),1244.00 (CH = = CH),1091.63 (N = H); ^{1}H NMR (Acetone-d6, 300 MHz, δ ppm): 6.9–7.2 (m,5H,phenyl); 7.20 (d, 2H, benzylidene); 7.22 (d, 2H, benzylidene); 6.70 (s, 1H, C = CH); 8.38 (s, 1H, NH); Mass (m / z) 390.1 (M^+). Anal. Calcd ($C_{16}H_{11}ClN_2OS$): C, 61.02; N, 8.70; S, 10.19 [Table 2].

5-(4-Methylbenzylidene)-2-(phenylimino) thiazolidin-4-one (X)

Yield: 62.00%, m.p: 202–204, R_f value (T: E: F; 5:4:1): 0.72, IR (KBr) cm^{-1}: 1550.94 (CH_2-CH_2) ,1770.60 (C = O), 3038 (Ar C–H), 2954 (aliphatic C–H) , 1337.22 (N-CH_2), ^{1}H NMR (Acetone-d6, 300 MHz, δ ppm): 2.08 (s, 3H, CH_3); 6.89–7.23 (m, 5H, phenyl); 7.36 (d, 2H, benzylidene); 7.51 (d, 2H, benzylidene); 7.76 (s, 1H, C = CH); 7.8 (s, 1H, NH). Mass (m / z) 294 (M^+) [Table 2].

5-(2-hydroxy-5-methylbenzylidene)-2-(phenylimino) thiazolidin-4-one (XI)

Yield: 71.10%, m.p: 239-241, R_f value (T: E: F; 5:4:1): 0.77, IR (KBr) cm^{-1}: 1530.94 (CH_2-CH_2), 1670.60 (C = O), 3565 (O–H), 3029 (Ar C–H), 1357.22 (N-CH_2). ^{1}H NMR (Acetone-d6, 300 MHz, δ ppm): 6.71–7.31 (m, 9H, phenyl and benzylidene); 7.69 (s, 1H, C = CH); 8.40 (s, 1H, NH); 9.85 (s, 1H, OH). Mass (*m / z)* 296 (M^+) [Table 2].

5-(4-nitrobenzylidene)-2-(phenylimino) thiazolidin-4-one (XII)

Yield: 54.50%, m.p: 320–322, R_f value (T: E: F; 5:4:1): 0.73, IR (KBr) cm^{-1}: 1515.94 (CH_2-CH_2) ,1660.60 (C = O), 1346.22 (N-CH_2) ,^{1}H NMR (Acetone-d6, 300 MHz, δ ppm): 6.99–7.04 (m, 5H, phenyl; 7.63 (s, 1H, C = CH); 7.58 (m, 2H, 4-nitrobenzylidene); 8.21 (m, 2H, 4-nitrobenzylidene); 8.44 (s, 1H, NH), Mass (m / z) 586.1 (M^+). Anal. Calcd. ($C_{16}H_{11}N_3O_3S$): C, 59.07; N, 12.90; S, 9.80 [Table 2].

5-(2-chlorobenzylidene)-2-(phenylimino) thiazolidin-4-one (XIII)

Yield: 82.80%, m.p: 200 – 202, R_f value (T: E: F;

5:4:1): 0.65, IR (KBr) cm^{-1}: 1520 (CH_2-CH_2), 1670 (C = O), 1070 (N-CH_2) , ^1H NMR (Acetone-d6,300 MHz, δ ppm): 6.99 – 7.0 (m, 5H, phenyl); 7.20 (s, 1H, C = CH); 7.00 – 7.20 (m, 4H, chlorobenzylidene); 8.2 (s, 1H, NH) Mass spectra (m / z) 314.02 (M^+). Anal. Calcd ($C_{16}H_{11}ClN_2OS$): C, 61.04; N, 8.80; S, 10.19 [Table 2]

5-(phenoxymethylene)-2-(phenylimino) thiazolidin-4-one (XIV)

Yield: 61.00%, m.p: 280-282, R_f value (T: E: F; 5:4:1): 0.78, IR (KBr) cm^{-1}: 1670.24 (C = O), 1240.14 (CH = CH), 1176.50 (N = H); ^1H NMR (Acetone-d6, 300 MHz, δ ppm): 6.91 – 7.01 (m, 5H, phenyl) 6.89 (s, 1H, C = CH); 6.89-7.01(Ar C-H benzylidene); 7.36 (s, 1H, NH), Mass (m / z) 525.0 (M^+). Anal. Calcd ($C_{16}H_{12}N_2O_2S$): C, 64.80; N, 9.40; S, 10.80 [Table 2].

5-(2, 4-difluorobenzylidene)-2-(phenylimino) thiazolidin-4-one (XV)

Yield: 60.50%, m.p: 240-242, R_f value (T:E:F; 5:4:1): 0.62; IR (KBr) cm^{-1}: 3468 (N-H); 3025 (Ar C-H); 1674 (C = O); 1608 (C = N); 1038 (C-F); ^1H NMR (Acetone-d6,300 MHz, δ ppm): 6.99-7.00 (m, 5H, phenyl); 7.00 (s, 1H, C = CH); 8.2 (s, 1H, NH); 6.60-7.25 (Ar C-H benzylidene); Mass (m / z) 316.04 (M^+). Anal. Calcd ($C_{16}H_{10}F_2N_2OS$): C, 6.072; N, 8.80; S, 10.10 [Table 2].

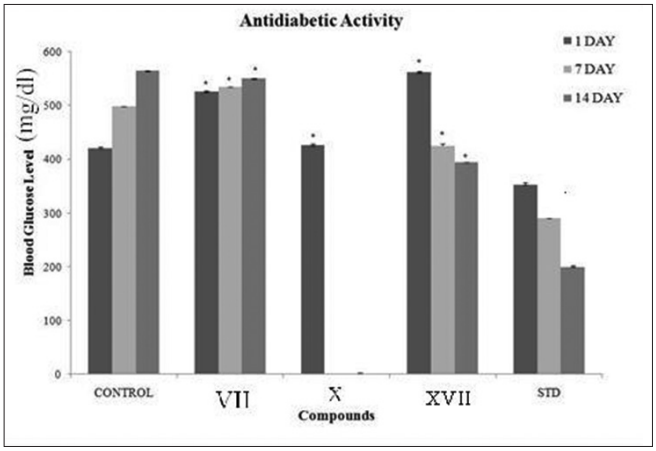


Figure 3: Antidiabetic Activity of Synthesized Compounds at a Dose of (200 mg / kg) in albino mice, All the values are expressed as Mean ± S.E.M (n = 6). *$P \leq 0.05$ and **$P \leq 0.01$, ***$P \leq 0.001$ indicates the level of significance when compared with the control

5-(2-fluorobenzylidene)-2-(phenylimino) thiazolidin-4-one (XVI)

Yield: 82.20% m.p: 260 – 262, R_f value (T: E: F; 5:4:1): 0.76, IR (KBr) cm^{-1}: 3252.43 (N-H), 1616.94 (C = N), 1548.60 (C = C), 1513.33, 1447.40, and 1048.88; ^1H NMR (Acetone-d6, 300 MHz, δ ppm): 6.99-7.00 (m, 5H, phenyl); 7.00 (s, 1H, C = CH); 8.2 (s,1H, NH); 6.80 – 7.25 (Ar C-H benzylidene); Mass (m / z) 296.06 (M^+). Anal. Calcd ($C_{16}H_{11}FN_2OS$): C, 64.40; N, 9.30; S, 10.74 [Table 2].

5-(2, 4-dinitrobenzylidene)-2-(phenylimino) thiazolidin-4-one (XVII)

Yield: 51.40% m.p: 242 – 244, R_f value (T: E: F; 5:4:1): 0.74, IR (KBr) cm^{-1}: 1664 (C = O), 1160 (C = CH), 670 (Ar str), 1340 (NO_2 str); 1608 (C = N); ^1H NMR (Acetone-d6, 300 MHz, δ ppm): 6.99-7.00 (m, 5H, phenyl); 7.32 (s, 1H, C = CH); 8.2 (s, 1H, NH); 7.80–9.00 (Ar C-H benzylidene) Mass (m / z) 370.02 (M^+). Anal. Calcd ($C_{16}H_{10}N_4O_5S$): C, 51.89; N, 15.12; S, 8.60 [Table 2].

5-(2-bromobenzylidene)-2-(phenylimino) thiazolidin-4-one (XVIII)

Yield: 78.20% m.p: 270–272, R_f value (T: E: F; 5:4:1): 0.60, IR (KBr) cm^{-1}: 1384.79 (C = C), 756.04 (C-H Ar), 686.61 (C-Br), ^1H NMR (Acetone-d6,300 MHz, δ ppm): 6.99 – 7.00 (m, 5H, phenyl); 7.37 (s,1H, C = CH); 8.0 (s, 1H, NH); 7.34–7.42 (Ar C-H benzylidene), Mass (m / z) 572.9 (M^+). Anal. Calcd. ($C_{16}H_{11}BrN_2OS$): C, 53.48; N, 7.80; S, 8.90 [Table 2].

Antidiabetic activity

Animal

Albino-Swiss rats weighing (150 – 200 g) were used for studying *in-vivo* antidiabetic activity. Animals were maintained under standard laboratory conditions (24 ± 2°C; relative humidity 60 – 70%). A study protocol was approved by the Institutional Animal

Table 3: Antidiabetic activity of the synthesized compound

Compounds	Average Serum Glucose Level (mg / dL)		
	First day	Seventh day	Fourteenth day
Control	421 ± 1.52	498 ± 0.57	564 ± 1.20
Standard	353 ± 1.15	291 ± 0.57	472 ± 0.88
VII	526 ± 2.47	534 ± 3.53	550 ± 3.53
X	426 ± 1.31	-	-
XVII	561 ± 3.25	425 ± 2.50	395 ± 2.50

All values are expressed in Mean ± SEM of six animals in each group. (-) indicates that the animals died during the experiment.

Ethics Committee for the Purpose of Control and Supervision of Experiments on Animals (IAEC, Approval No.711 / 02 / a / CPCSEA) before the experiment. Albino-Swiss rats from the Laboratory Animal House Section, Department of Pharmaceutical Technology, Meerut Institute of Engineering and Technology, Meerut, were used in the study. The animals were kept in polypropylene cages and maintained on balanced ration with free access to clean drinking water.

Induction of diabetes mellitus

Streptozotocin (STZ) was obtained from sigma chemicals (USA). STZ was dissolved in cold 0.01 M citrate buffer, pH 4.5 and prepared freshly for immediate use. The animals were fasted for 20 hours and then the STZ injection was given intraperitoneally at a dose of 60 mg / kg. The blood glucose concentration was measured on the first day, seventh day, and fourteenth day, with the help of a glucometer, by using a blood sample from tail vein.

Experimental groups and protocol

The animals were divided into standard, test, and control. The test drug was suspended in 1% Na-CMC (Na-Carboxymethyl cellulose) and administered at a dose of 200 mg / kg orally. Subsequently, the serum glucose level was determined and is reported in Table 3 and the graphical data in Figure 3.

RESULTS

The structures of the synthesized compounds were confirmed by IR spectra, ^{1}HNMR spectral analysis, and mass and elemental analysis. The IR spectra exhibited some characteristic bands due to = C-H str. (3100 – 3000 cm/1), C = C str. (1635 – 1495 cm/1), C-H bending (900 – 860 cm/1), C-H bending (substituted aryl (840 – 800 cm/1), C-Cl str. (750 – 700 cm/1), C-F str. (1100 – 1000 cm/1), C-S-C str. (700 – 600 cm/1), C = N (ring) (1650 – 1580 cm/1) stretching vibration band, and C = O (1674 cm/1, 4-thiazolidinone moiety). In the ^{1}H NMR spectra the signals appeared between δ 5.1 and 6.1 indicating the presence of thiazolidinone.

CONCLUSION

The tested compounds 5-(4-fluorobenzylidene)-2-(phenylimino) thiazolidin-4-on (VII) and 5-(4-Methylbenzylidene)-2-(phenylimino)thiazolidin-4-one (X), 5-(2, 4-dinitrobenzylidene)-2-(phenylamino) thiazolidin-4-one (XVII) were found to be ineffective in lowering the blood glucose level.

ACKNOWLEDGMENT

The authors are thankful to CDRI, Lucknow, for the spectral analyses of newly synthesized compounds and the Niscair laboratory for the literature survey.

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How to cite this article: Singh T, Sharma PK, Kumar N, Dudhe R. Absence of antidiabetic activity in some novel thiazolidinone derivatives. J Pharm Negative Results 2013;4:39-45.

Source of Support: Nil. **Conflict of Interest:** None declared.