Table 4: Docking analysis report with human pancreatic alpha amylase enzyme (4GQR) and peroxisome proliferator-activated receptor gamma (PPARgamma) (1FM6)

SL:No.	**Ligand**	**Docking score**	**Interacting Residue 4GQR**	Docking score	Interacting Residue**(1FM6)**
1	SA01	54.5996	Trp59, Asp197, Glu233 (3WHB)	81.12	Met364,Ser289, Arg288,His323
2	SA02	50.9353	No H bond interaction	71.42	Met364, Ser289
3	**SA03**	**64.7517**	Ala198, A:His201, Ala198	76.15	Met364, ser289
4	**SA04**	**63.3986**	Trp59, Asp197, Asp197, Glu233	**94.54**	Gln286,Ser289, Arg288,Phe282 (Whb)
5	SA05	54.1312	Asp197	73.68	Met364,Ser289
6	SA06	59.1726	His201	87.49	Tyr473, Gln286
7	**SA07**	**68.025**	Trp59 whb	**95.50**	His449, Ser289

Table 5: Report of *in vitro* antidiabetic screening.

µl/ml	**% of inhibition(Each value expressed as Mean±SEM)**							
	Acarbose	**SA01**	**SA02**	**SA03**	**SA04**	**SA05**	**SA06**	**SA07**
25	24.35	40.46±3.65	29.09±2.56	69.09±3.89	35.52±1.17	12.4±1.483	37.45±2.73	83.64±2.34
50	48.71	47.15±0.85	37.4±3.93	85.45±3.22	42.47±1.61	30.15±4.47	39.79±2.06	87.27±2.23
75	76.92	51.83±4.09	46.82±2.27	90.91±2.46	64.09±1.94	47.61±2.58	41.13±1.93	89.09±2.87
100	93.58	54.18±4.61	53.5±1.89	94.55±1.80	76.44±0.98	56.34±2.56	45.15±1.24	92.73±1.53

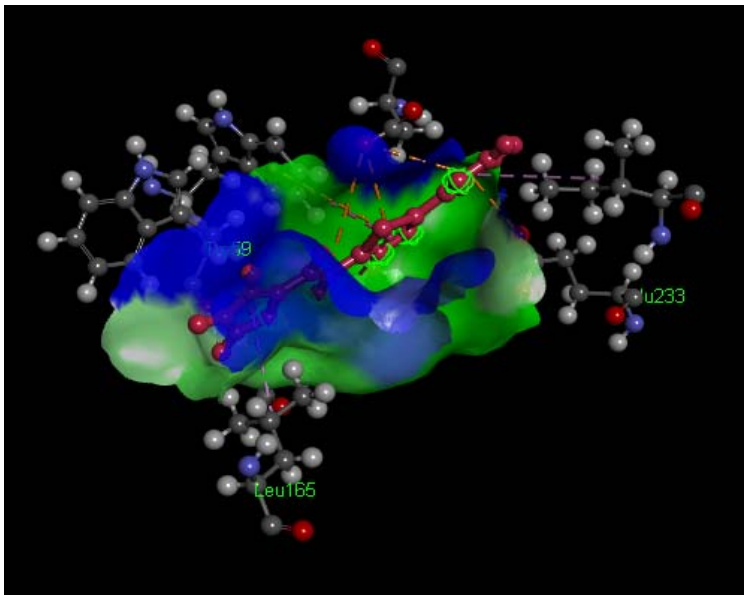

Fig 1: 3D view

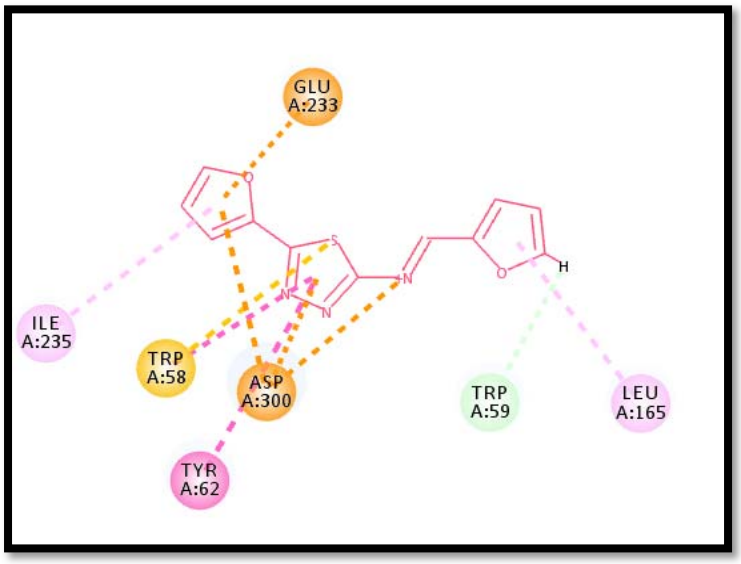

Fig 2: 2D view

Interaction of SA07 which have maximum docking score with 4GQR were shown in figure 1 and 2

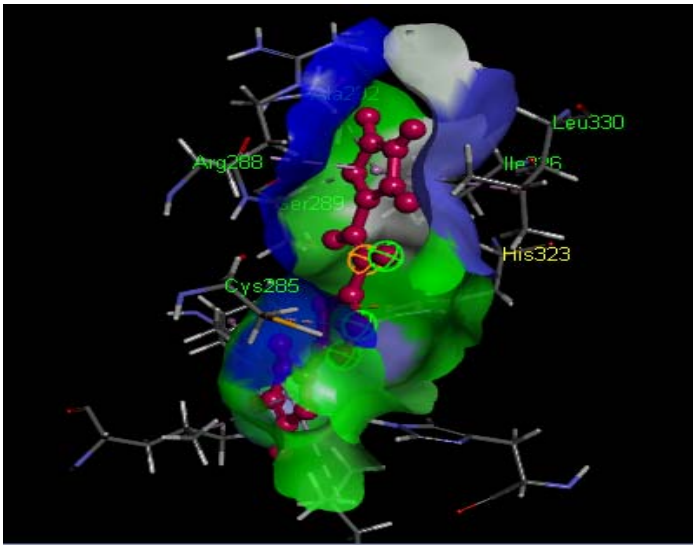

Fig 3: 3D view

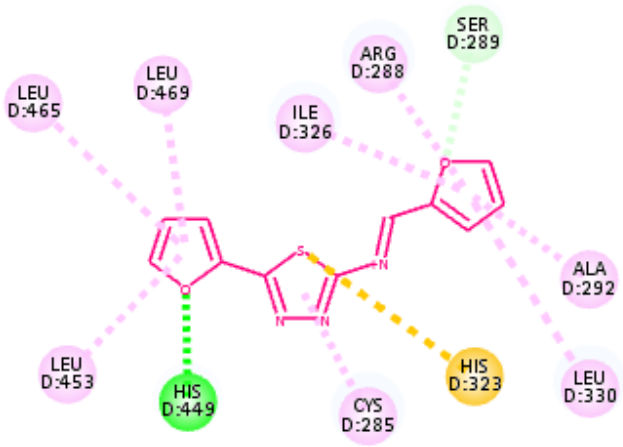

Fig 4: 2D view

Interaction of SA07 which have maximum docking score with 1FM6 were shown in figure 3 and 4

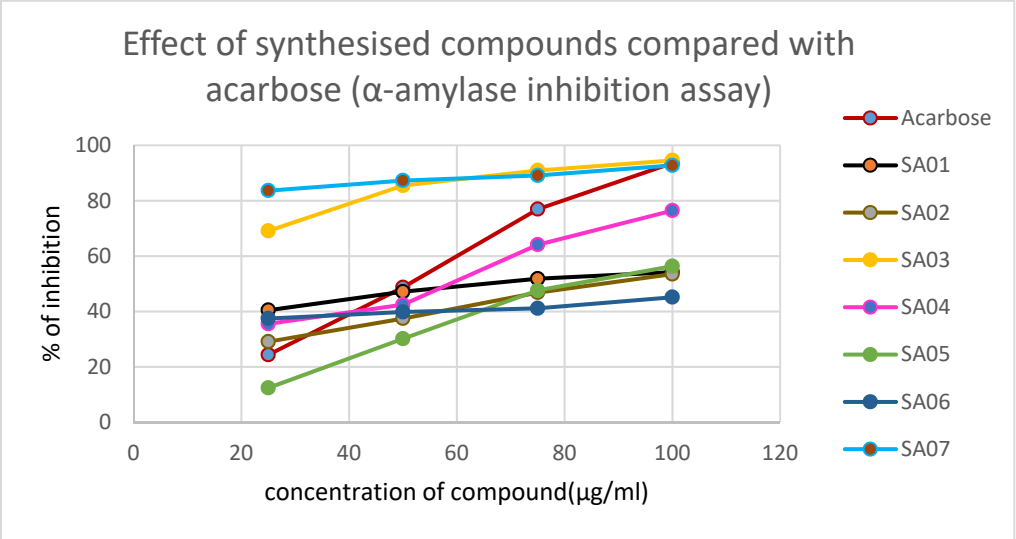

Figure 5: Comparison of percentage of inhibition shown by synthesised compounds.

CONCLUSION

The designed and synthesized 5-furyl-1,3,4-thiadiazol-2-imine derivatives showed good docking score and *in vitro* anti-diabetic activity. *In silico* physico chemical prediction studies confirmed that the majority of the title compounds possessed the druglikeness character. *In vitro* screening results suggested that compounds in which phenyl ring with electron donating groups at 2, 4th position (SA03) and that with furyl ring (SA07) attached to imine linkage exhibited significant alpha-amylase inhibitory activity. The docking studies with PPAR gamma receptor proved that the proposed compound SA07 and SA04 have best docking score, thus giving insight to antidiabetic activity after systemic absorption also. Compounds namely SA03, SA07 and SA04 having significant docking score and percentage of inhibition, can be selected for further optimisation and can be explored for *in vivo* activity in the mere future thus resulting in the development of novel anti-diabetic drugs with better pharmacological profile.

CONFLICT OF INTERESTS:

The authors declare that there is no conflict of interests regarding the publication of this paper.

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REFERENCES

[1] Wild S, Roglic G, Green A, Sicree A, King H. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care. 2004; 27(5): 1047–1053.
[2] Vidhya, Renitta. Evaluation of antihyperglycemic and antihyperlipidemic activities of an edible gastropod (Achatina fulica) in alloxan-induced diabetic mice. Asian J Pharm Clin Res. 2016; 9(3]): 206-211.
[3] Pattan SR, Kekare P, Dighe NS, Nirmal SA, Musmade DS, Parjane SK, et al. Synthesis and biological evaluation of some 1, 3, 4-thiadiazoles. J. Chem. Pharm. Res. 2009; 1(1): 191-198.
[4] Baron AD. Postprandial hyperglycaemia and α-glucosidase inhibitors. Diabetes Res Clin Pract. 1998; 40 (1): S51-S55.
[5] Sindhu. SN, Kavrekar V, Mishra A. In vitro studies on alpha amylase and alpha glucosidase inhibitory activities of selected plant extracts. Euro. J. Exp. Bio. 2013; 3(1):128-132.
[6] Visagaperumal D, Ramalingam J, Chandy V. 1, 3, 4-Thiadiazoles: An Overview. Curr Res Bioorg Org Chem. 2018; 103. DOI: 10.29011/CRBOC -101. 100003.
[7] Serban G, Stanasel O, Eugenia S, Bota S. 2-Amino-1,3,4-thiadiazole as a potential scaffold for promising antimicrobial agents. Drug Des. Dev. Ther. 2018; 12: 1545–66.
[8] Shrivastava K, Purohit S, Singhal S. Studies On Nitrogen and Sulphur Containing Heterocyclic Compound: 1,3,4 - thiadiazole. Asian J Biomed Pharmaceut Sci 2013; 3(21): 6-23.
[9] Karigar AA, Himaja M, Malisunil V, Jagadeesh PK. One Pot Synthesis and Antitubercular Activity of 2-Amino-5-Aryl-5H-Thiazolo (4,3-B) 1,3,4- Thiadiazoles. IRJP. 2011; 2(1): 153-158.
[10] Syed MA, YRP Reddy, Chandrasekhar KB. Design, one pot synthesis and biological evaluation of imidazo[2,1-b] [1,3,4]-thiadiazole derivatives for their antitubercular and antifungal activity. J of Applied Pharm.Sci. 2018; 8(07): 021-027.
[11] Kamal M, Shakya AK, Jawaid T. 1,3,4-thiadiazole as antiinflammatory agent: a review. IJCRR.2001; 2(11): 14-26.
[12] Banerjee R, Roy D, Banerjee M. Synthesis, wound healing and diuretic activity of some new 1, 3, 4 thiadiazole derivatives. WJPPS.2015; 4(11): 1769-1778.
[13] Datar PA, Deokule TA. Design and synthesis of thiadiazole derivatives as antidiabetic agents. Med chem. 2014; 4: 390-399.

[14] Raj V, Rai A, Singh M, Kumar R, Kumar A, Kumar S, and Sharma SK. Recent update on 1,3,4-thiadiazole derivatives: as anticonvulsant agents. ARJPM. 2015; 1(1): 34-61.
[15] Malleshappa NN, Patel HM, Singh N, Gadad AK, Cameotra SS and Badiger A. Synthesis and anticancer evaluation of novel 2-cyclo propyl imidazo[2,1-b]1,3,4-thiadiazole derivatives. Eur J of Med Chem. 2011; 49(9): 4411-18.
[16] Sherin AH, Joyamma V, Jayasekhar P. Schiff bases and Bicyclic derivatives comprising 1, 3, 4-thiadiazole moiety- A Review on their Pharmacological activities. Asian J. Pharm. Res. 2019; 9(4): 299-306.
[17] Gadhiya B, Rajput M, Atul B, Kartik L. Design, synthesis and evaluation of antimicrobial activities of some novel thiazole and thiadiazole derivatives clubbed with 1Hbenzimidazole.RASAYAN. J.CHEM. 2016; 9(3): 355-372.
[18] Rakesh Y, Divya Y, Sarvesh KP. Novel biphenyl imidazo[2,1- b][1,3,4]-thiadiazole -a versatile scaffold. DHR-IJPS. 2012; 2(1): 20-37.
[19] Bibi S, Sakata. K Current Status of Computer-Aided Drug Design for Type 2 Diabetes. Curr Comput Aided Drug. 2016; 12: 167-177.
[20] Oprea TI. Virtual Screening in Lead Discovery: A Viewpoint. Molecules. 2002; 7: 51–62.
[21] Rajasekhar KK. Abdrrahman SS, Mekonnen YT, Padmavathamma M, Ranganayakulu D, Shankarananth V. In silico prediction of biological activity, selected pharmacokinetic and toxicity profile of some 2,4,6-trisubstituted pyrimidines derived from guanabenz and guanfacine. IJIPR. 2015; 6(2): 468-477.
[22] ACD labs Chem sketch. ver 12.0 for Windows, Advanced Chemistry Development Inc, Toronto, Canada, http://www.acdlabs.com.
[23] Ravi KK. Giri A, Nadendla RR. In silico Adme Profiling of Cdk9 Inhibitors. J Sci Res Pharm. 2018;7(3):30-34.
[24] "Osiris Property Explorer.": ‹http://www.organic-chemistry.org/ prog/peo/›
[25] "PASS (Prediction of Activity Spectra for Substances) program"., http://www.way2drug.com/passonline.
[26] Atta KFM, Omaima OM, Farahat, Alaa ZA, Ahmed, Marei MG, Synthesis and antibacterial activities of novel imidazo[2,1-b]-1,3,4-thiadiazoles. Molecules. 2011;16: 5496-5506.
[27] Pandey A, Rajavel R, Chandraker S, Deepak D. Synthesis of schiff bases of 2-amino-5-aryl-1,3,4- thiadiazole and its analgesic, anti-inflammatory and anti-bacterial activity. J Chem. 2012; 9(4): 2524-2531.
[28] Ganesan MS, Raja KK, Narasimhan K, Murugesan S, Karan KB. Design, synthesis, a-amylase inhibition and in silico docking study of novel quinoline bearing proline derivatives. J. Mol. Struct. 2020; 1208: 127873.
[29] Merlin NJ, Sandhya MJN, Janeera B, Shaji SD et al. In-silico design, synthesis and in-vitro antidiabetic and anti-inflammatory activities of 1,3,4-thiadiazole substituted 2-methyl benzimidazole derivatives. JPRCP. 2016; 6(1): 27-38.