International Journal of Biomedical Investigation

journal homepage: https://ijbi.edwiserinternational.com

Original Article

Novel 2,4-Thiazolidinedione Derivatives as Potential Therapeutics for NAFLD: Molecular Design, Synthesis, and Biological Validation Targeting FFAR4

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ARTICLE INFO

Received 22 June 2025
Revised 01 August 2025
Available Online 05 August 2025

Keywords:
FFAR4
NAFLD
Inflammation
Lipid metabolism
2,4-Thiazolidinedione

ABSTRACT

Aim: To design, synthesize, and biologically validate novel 2,4-thiazolidinedione derivatives as potential FFAR4 modulators for the treatment of non-alcoholic fatty liver disease (NAFLD).
Objective: This study aims to investigate the interactions between synthesized thiazolidinedione derivatives and the FFAR4 binding site, assess their lipid-lowering efficacy, and evaluate their safety profiles in vitro.
Method: In silico molecular docking studies were conducted to identify potential interactions between the derivatives and the FFAR4 binding site, followed by the synthesis of selected compounds using conventional methods. Comprehensive physicochemical characterization was performed using UV, FTIR, NMR, and mass spectrometry. In vitro evaluations included lipid accumulation assays using hepatocyte cell lines and cytotoxicity assessments via MTT assays.
Result: The docking studies revealed favourable binding affinities with key amino acid residues in FFAR4, guiding the rational design of lead compounds. The synthesized derivatives demonstrated significant lipid-lowering activity in hepatocyte cell lines, with several compounds exhibiting promising safety profiles in cytotoxicity tests.
Conclusion: The results support the hypothesis that 2,4-thiazolidinedione derivatives can effectively act as FFAR4 agonists, contributing to reduced lipid accumulation in hepatocytes. This study underscores the potential of these derivatives as therapeutic agents for NAFLD, highlighting the importance of further development and clinical evaluation in addressing this critical health concern. The integrated approach utilized here provides a valuable foundation for advancing the discovery of novel FFAR4-targeted agents in the fight against metabolic liver diseases.

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https://doi.org/10.31531/2581-4745.1000169

Introduction

Disease Target

The term non-alcoholic fatty liver disease (NAFLD) was first introduced by Schaffner in 1986. NAFLD is now recognized as the leading cause of chronic liver disease globally, constituting a significant and often overlooked public health crisis [1]. Current estimates indicate that approximately 25% of the general population suffers from NAFLD, with 3-5% affected by non-alcoholic steatohepatitis (NASH) [2].

NAFLD is characterized by excessive fat accumulation in the liver among individuals who consume little to no alcohol, ranging from simple fatty liver (steatosis) to more severe forms like NASH, which can lead to liver fibrosis, cirrhosis, and hepatocellular carcinoma [3]. This condition is closely associated with metabolic disorders, including obesity, type 2 diabetes mellitus (T2DM), dyslipidemia, and hypertension [3-5]. Symptoms are frequently absent or nonspecific, such as fatigue or abdominal discomfort, which complicates early diagnosis [6].

At present, there is no approved pharmacological treatment specifically for NAFLD. However, potential therapeutic options include insulin sensitizers, weight loss medications (such as rimonabant, a cannabinoid [CB1] receptor inhibitor), lipid-lowering agents (including statins and fibrates), and hepatoprotective antioxidants (like vitamin E, ursodeoxycholic acid, betaine, and lipoic acid) [6-8].

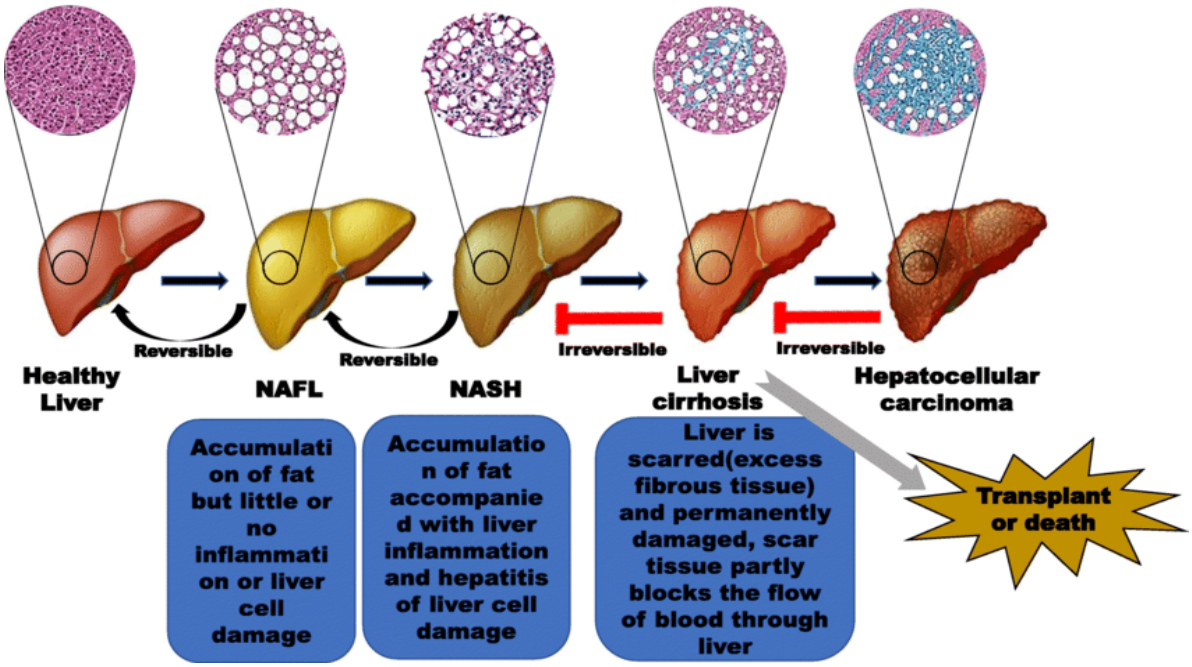


Figure 1: Clinical progression of NAFLD/NASH.

Biological Target

The Free Fatty Acid Receptor 4 (FFAR4), also referred to as GPR120, is pivotal in regulating inflammation by modulating pro-inflammatory cytokine release and enhancing insulin sensitivity [9]. FFAR4 is activated by long-chain fatty acids, initiating powerful anti-inflammatory signaling pathways. Upon activation, FFAR4 effectively inhibits the Toll-like receptor (TLR)-mediated activation of NF-κB and significantly reduces the production of pro-inflammatory cytokines such as TNF-α and IL-6. This anti-inflammatory action is mediated via β-arrestin-2-dependent signaling, which also enhances insulin sensitivity [10].

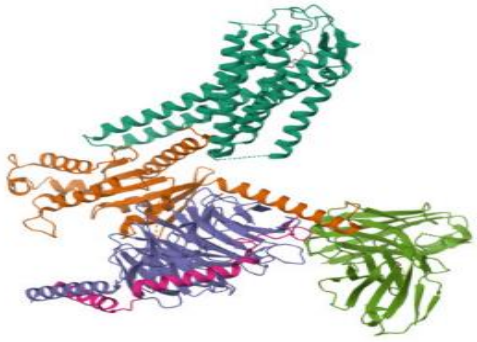


Figure 2: 3D Structure of FFAR4 (8ID6).

Drug Design

Drug design, often called rational drug design, is an innovative process for developing new drug molecules based on known interactions with biological targets [11].

Computational methods ideally predict the binding affinity of compounds prior to synthesis, allowing researchers to focus on the most promising candidates, thereby saving significant time and resources. These computational techniques have transformed the discovery process by reducing the number of required iterations and consistently yielding novel structures [12,13].

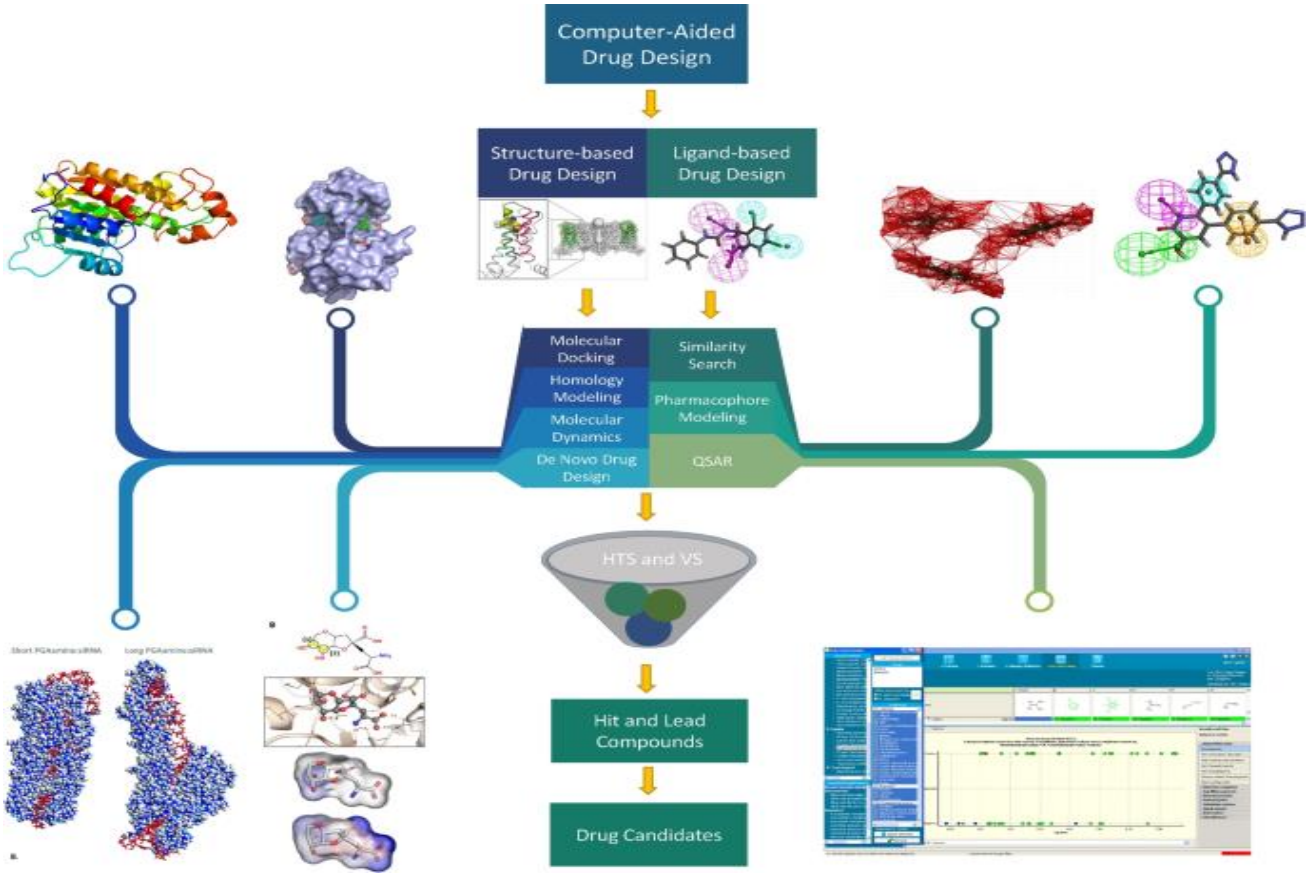


Figure 3: Computer-Aided Drug Design.

Chemistry of Scaffold

2,4-Thiazolidinedione (TZD) is a distinctive five-membered heteroaryl ring structure, featuring nitrogen and sulfur atoms alongside two adjacent carbonyl groups. It stands out as a highly privileged scaffold for developing pharmaceutically active compounds [14-16].

2,4-TZD derivatives are well-established for their anti-inflammatory and insulin-sensitizing properties. The administration of TZD influences the production of adipokines and lowers pro-inflammatory cytokines, particularly TNF-α, which correlates positively with the degree of steatosis and fibrosis [17-19].

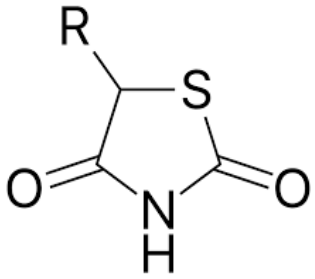


Figure 4: Structure of 2,4 Thiazolidinedione.

Materials and Methods

Target Selection

Based on the literature review, FFAR4 (PDB ID - 8ID6) was chosen as the target.

Scaffold Selection

2,4-thiazolidinedione was chosen as the basic nucleus. Structural modification at 3 and 5 positions was done to get novel compounds.

Designing Of Novel Compounds

About 162 ligands were designed using Chemsketch software.

Novelty Assessment

Novelty of those ligands were assessed using Pubchem and Zinc15 database.

***In-Silico* Drug-Likeness & Toxicity**

Drug-likeness property and Toxicity profile of those ligands were evaluated using Molinspiration, a free web tool and Osiris Property explorer respectively.

Molecular Docking

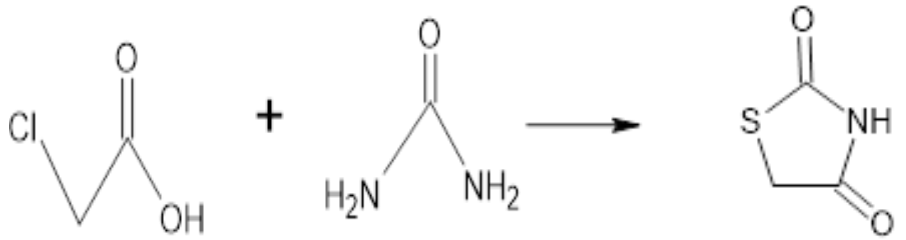
Energy minimization of the ligands was performed using Chem3D software. The energy minimized ligands were docked against the target using Autodock tools1.5.6. The interaction between the molecule and the target was viewed through Molegro Molecular viewer and Biovia Discovery Studio visualizer.

Synthesis

3 molecules (SN1C, SN15E, SN33C) were selected for further synthesis based on drug-likeness property, toxicity profile, optimum docking score and synthetic feasibility.

Synthetic Scheme [22-23]:

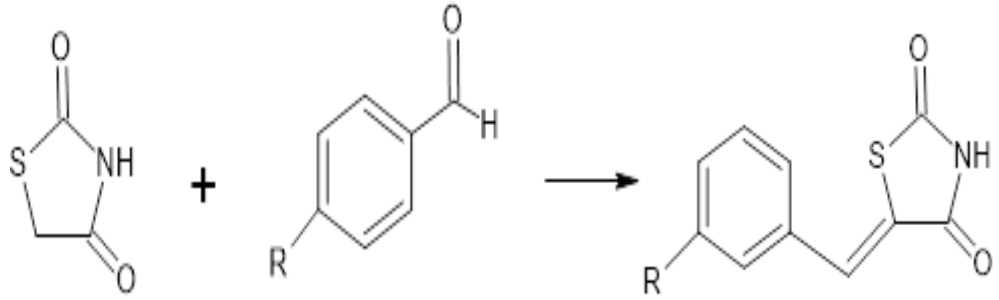
Step 1: Nucleus synthesis



Procedure

Chloroacetic acid (5.64g, 0.06 mol) in 6ml of H_2O + Thiourea (4.56g, 0.06 mol) in 6ml of H_2O - stirred for 15 mins - white solid precipitates - now slowly added 6ml of conc. HCl – stirred, refluxed for 10-12 hrs at 100-110˚C - on cooling - mass of clusters of white needles formed. The product is filtered, washed, dried, purified and recrystallized.

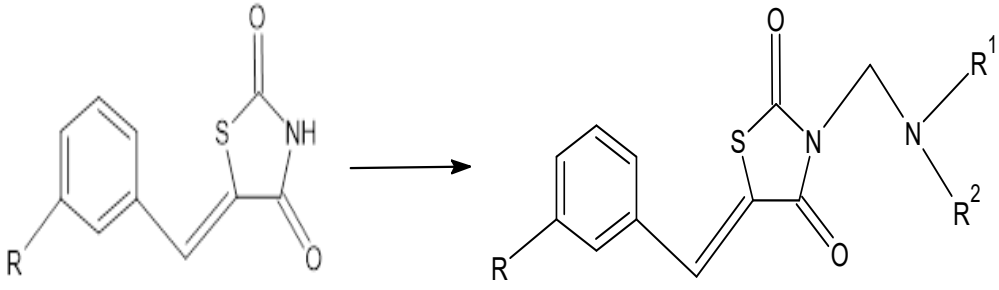
Step 2: Knoevenagel Condensation



Procedure

Thiazolidinedione (0.1mol) + Substituted benzaldehyde (0.1mol) + Toluene (10 ml) + catalyst – [piperidine (2-3 drops)] – stirred, refluxed at 110 ˚C for 8-10 hrs – on cooling, corresponding TZD derivatives precipitates. The product is filtered, washed, dried, purified and recrystallized.

Step 3: Mannich Reaction



Procedure

Benzylidene thiazolidinedione derivative (0.01 mol) + methanol (20ml) + formaldehyde (0.015 mol) - cooled to 0˚C – now add corresponding secondary amine (0.01 mol) – stirred for 3 hrs - left at room temperature for 24 hrs – final product precipitates. The product is purified and recrystallized.

Characterization

The synthesized compounds were characterized as follows: Melting point, Thin Layer Chromatography, UV spectroscopy, IR spectroscopy, IH-NMR spectroscopy, Mass spectrometry.

Biological Evaluation [24-28]

The synthesized compounds were evaluated for their activity against NAFLD using *in vitro* screening methods.

MTT cytotoxicity assay

MTT is cleaved by mitochondrial Succinate dehydrogenase and reductase of viable cells, yielding a measurable purple product formazan. This formazan production is directly proportional to the viable cell number and inversely proportional to the degree of cytotoxicity.

Free Fatty Acid induction & treatment

HepG2 cell lines were treated with a mixture of free fatty acids (oleic and palmitic acid) to induce lipid accumulation, mimicking NAFLD. Test compounds are then administered to assess their therapeutic effect.

Oil Red O staining

A fat-soluble dye used to stain and visualize intracellular lipid droplets. The intensity of red staining indicates the level of lipid accumulation and is used to evaluate the efficacy of treatment.

RT-PCR / Gene Expression Study

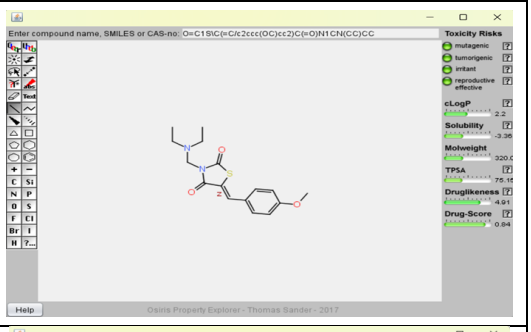
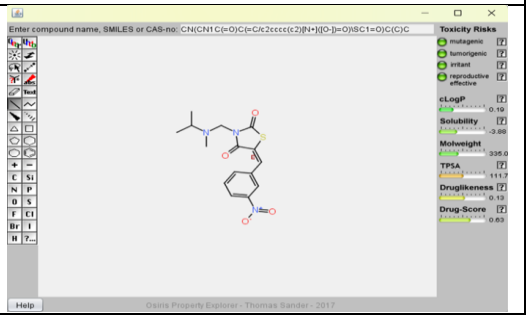
Reverse Transcription Polymerase Chain Reaction (RT-PCR) is a molecular technique used to measure the expression levels of specific genes. RNA is extracted from cells, converted into complementary DNA (cDNA), and then amplified using gene-specific primers. This allows quantification of gene expression changes, helping to assess the molecular effects of treatments or disease conditions.

Results And Discussion

In-Silico Studies

162 molecules were designed using *in-silico* method, out of which 3 molecules - **SN1C, SN15E, SN33C** were hand-picked for laboratory synthesis. It showed good affinity against the target FFAR4 and also possessed desired drug likeness and no toxicity in the computational tools.

Table 1: Novelty assessment and Toxicity prediction of synthesized compounds.

Compound ID	Novelty assessment	Toxicity prediction
SN1C	**Novel**	
SN15E	**Novel**	

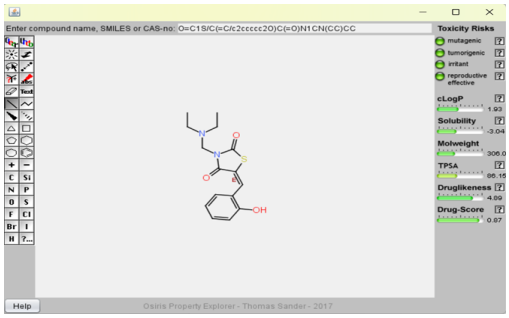
SN33C	**Novel**	

Table 2: Drug-likeness property of synthesized compounds.

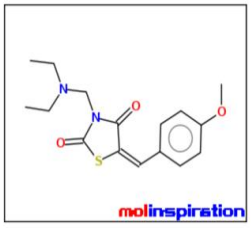
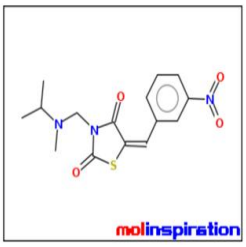
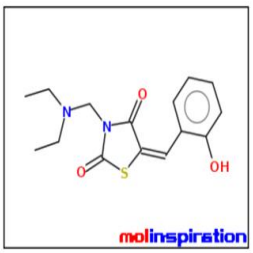
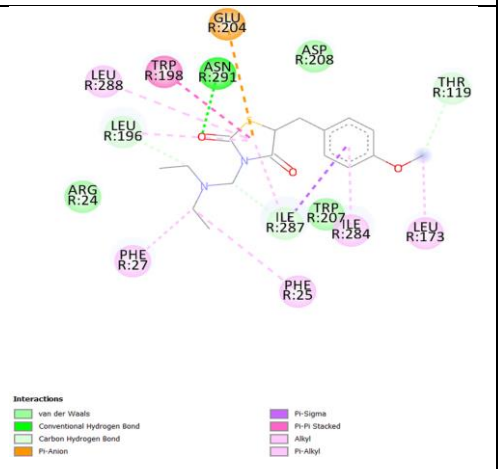
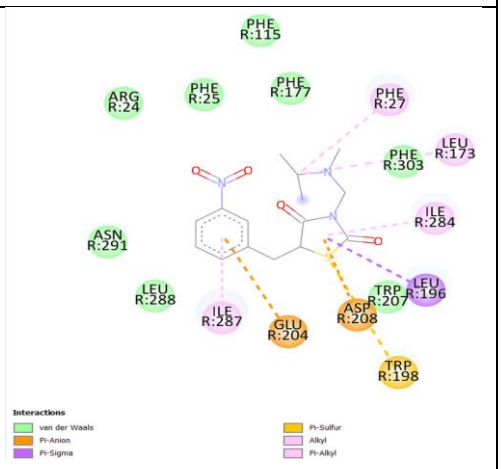
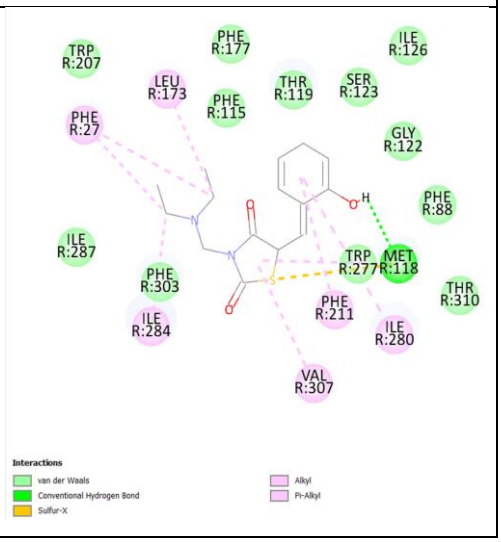
Compound ID	Drug-likeness property
SN1C	miSMILES: CCN(CC)Cn2c(=O)sc(=Cc1ccc(OC)cc1)c2=O  Molinspiration property engine v2022.08 miLogP 2.38 TPSA 51.55 natoms 22 MW 320.41 nON 5 nOHNH 0 nviolations 0 nrotb 6 volume 291.36
SN15E	miSMILES: [H]C(c1cccc(N(=O)=O)c1)=c2sc(=O)n(CN(C)C(C)C)c2=O  Molinspiration property engine v2022.08 miLogP 2.17 TPSA 88.14 natoms 23 MW 335.38 nON 7 nOHNH 0 nviolations 0 nrotb 5 volume 288.93
SN33C	miSMILES: [H]C(c1ccccc1O)=c2sc(=O)n(CN(CC)CC)c2=O  Molinspiration property engine v2022.08 miLogP 2.26 TPSA 62.54 natoms 21 MW 306.39 nON 5 nOHNH 1 nviolations 0 nrotb 5 volume 273.83

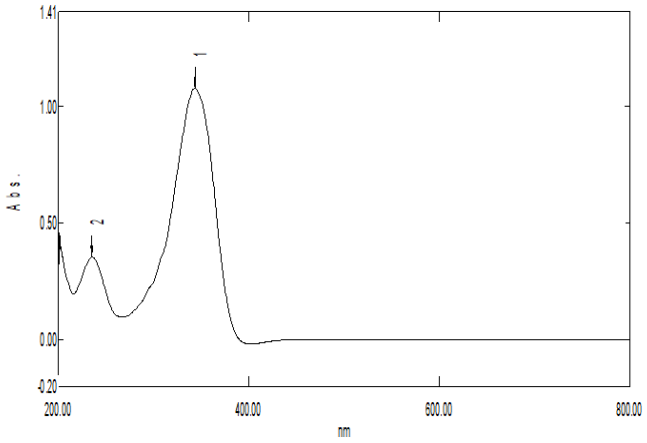
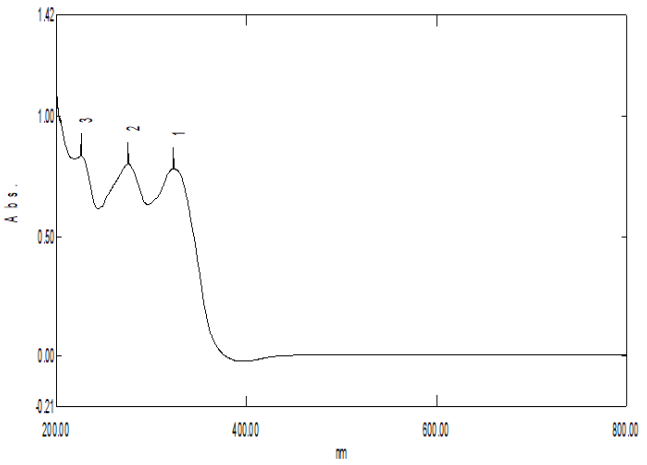
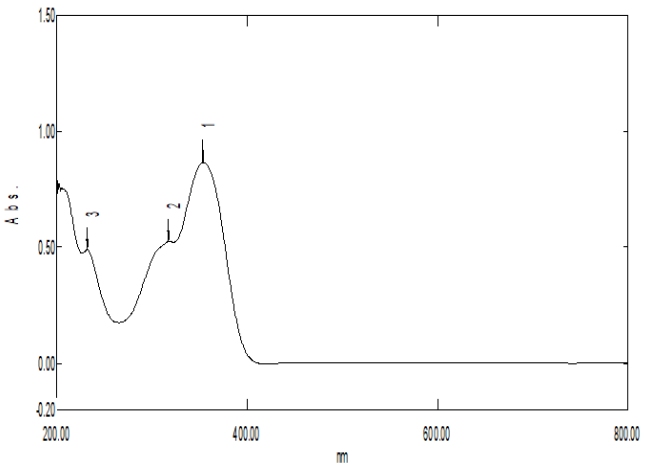
Table 3: Docking score and Docking interaction of synthesized compounds.

Compound ID	Docking score against biological target (Kcal/mol) FFAR4 (PDB ID:8ID6)	Docking interaction
SN1C	**-9.48**	
SN15E	**-8.9**	
SN33C	**-8.32**	

Characterization Studies

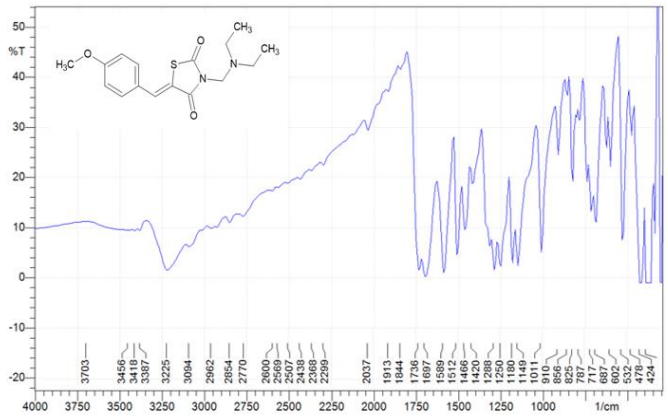
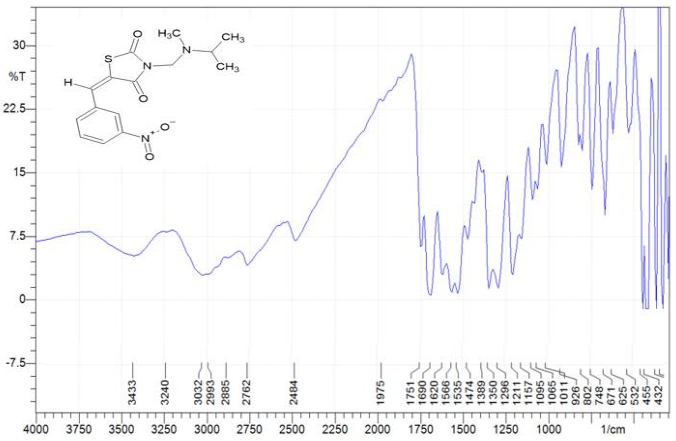
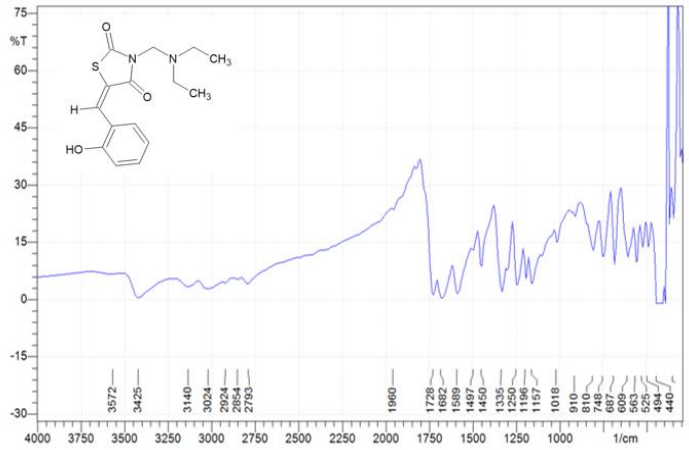
UV Spectroscopy

Table 4: UV spectrum of synthesized compounds.

Compound ID	UV Spectrum	λ_{max}
SN1C		**343.5 nm**
SN15E		**323.5 nm**
SN33C		**353.5 nm**

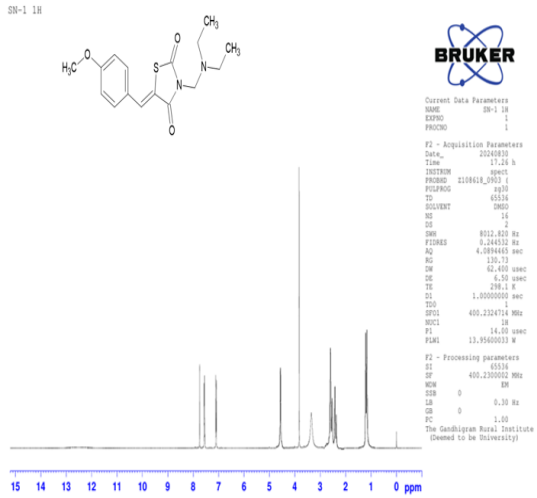
IR Spectroscopy

Table 5: IR spectrum of synthesized compounds.

Compound ID	IR Spectrum	Interpretation
SN1C		FUNCTIONAL GROUP / STRETCHING FREQUENCY (cm^{-1}) C-H (Aromatic) 3094 C-H (Aliphatic) 2962 C=C 1589 C=O 1697 C-N 1180 C-O 1011
SN15E		FUNCTIONAL GROUP / STRETCHING FREQUENCY (cm^{-1}) C-H (Aromatic) 3032 C-H (Aliphatic) 2993 C=C 1620 C=O 1690 C-N 1157 NO_2 1566
SN33C		FUNCTIONAL GROUP / STRETCHING FREQUENCY (cm^{-1}) C-H (Aromatic) 3024 C-H (Aliphatic) 2924 C=C 1589 C=O 1682 C-N 1157 O-H 3425

NMR Spectroscopy

Table 6: NMR spectrum of synthesized compounds.

<table>
<tr><th>Compound ID</th><th>NMR Spectrum</th><th>Interpretation</th></tr>
<tr><td>SN1C</td><td>  </td><td>
<table>
<tr><th>δ VALUE (PPM)</th><th>NATURE OF PROTONS</th><th>NATURE OF PEAKS</th><th>NUMBER OF PROTONS</th></tr>
<tr><td>7.85</td><td>1-ethylene -H</td><td>Singlet</td><td>1</td></tr>
<tr><td>7.63, 7.63</td><td rowspan="2">Aromatic C-H</td><td>Doublet</td><td rowspan="2">4</td></tr>
<tr><td>7.14, 7.14</td><td>Doublet</td></tr>
<tr><td>4.55</td><td rowspan="2">Methylene -CH₂</td><td>Singlet</td><td rowspan="2">6</td></tr>
<tr><td>2.64, 2.64</td><td>Quartet</td></tr>
<tr><td>3.81</td><td rowspan="2">Methyl -CH₃</td><td>Singlet</td><td rowspan="2">9</td></tr>
<tr><td>1.02, 1.02</td><td>Triplet</td></tr>
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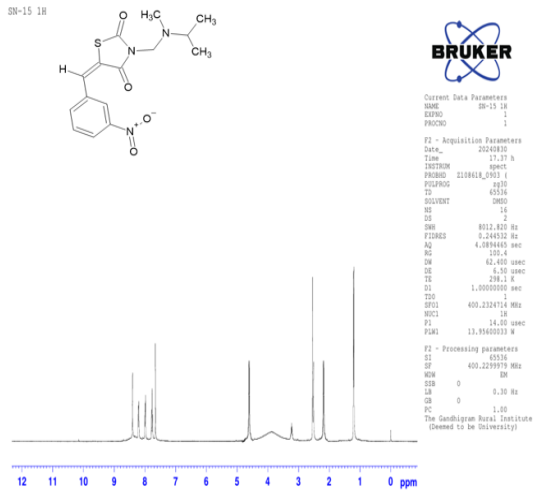
<tr><td>SN15E</td><td>  </td><td>
<table>
<tr><th>δ VALUE (PPM)</th><th>NATURE OF PROTONS</th><th>NATURE OF PEAKS</th><th>NUMBER OF PROTONS</th></tr>
<tr><td>8.49</td><td>1-ethylene -H</td><td>Singlet</td><td>1</td></tr>
<tr><td>7.87 – 8.27</td><td>Aromatic C-H</td><td>Multiplet</td><td>4</td></tr>
<tr><td>4.55</td><td>Methylene -CH₂</td><td>Singlet</td><td>2</td></tr>
<tr><td>2.69</td><td>Methine -CH</td><td>Multiplet</td><td>1</td></tr>
<tr><td>2.26</td><td rowspan="2">Methyl -CH₃</td><td>Singlet</td><td rowspan="2">9</td></tr>
<tr><td>1.00, 1.00</td><td>Doublet</td></tr>
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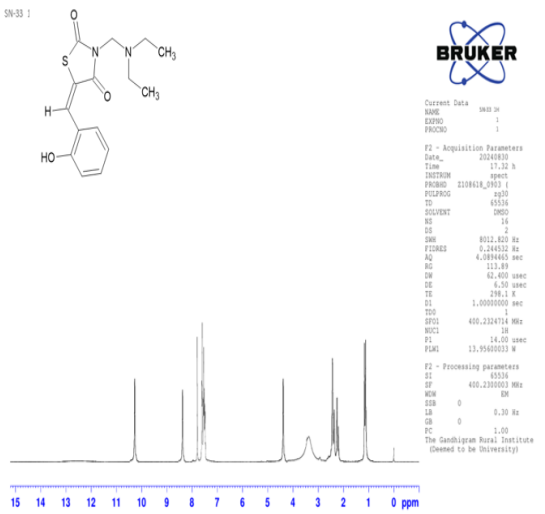
</td></tr>
<tr><td>SN33C</td><td>  </td><td>
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<tr><td>10.27</td><td>Alcohol -OH</td><td>Singlet</td><td>1</td></tr>
<tr><td>8.34</td><td>1-ethylene -H</td><td>Singlet</td><td>1</td></tr>
<tr><td>6.72 – 7.49</td><td>Aromatic C-H</td><td>Multiplet</td><td>4</td></tr>
<tr><td>4.55</td><td rowspan="2">Methylene -CH₂</td><td>Singlet</td><td rowspan="2">6</td></tr>
<tr><td>2.64, 2.64</td><td>Quartet</td></tr>
<tr><td>1.02, 1.02</td><td>Methyl -CH₃</td><td>Triplet</td><td>6</td></tr>
</table>
</td></tr>
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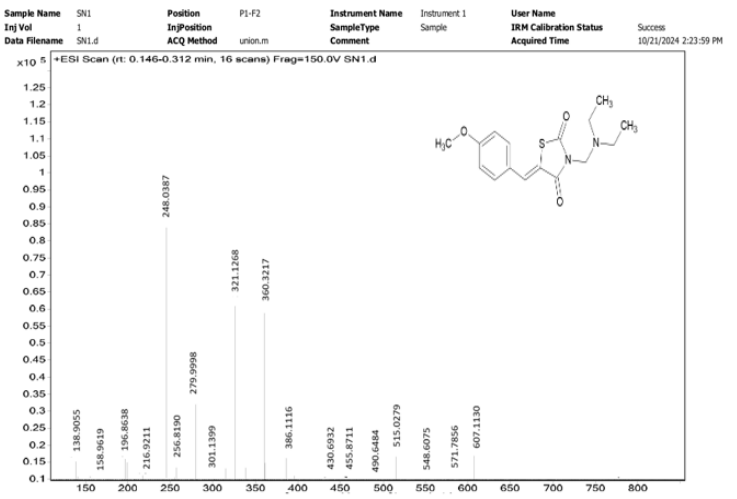
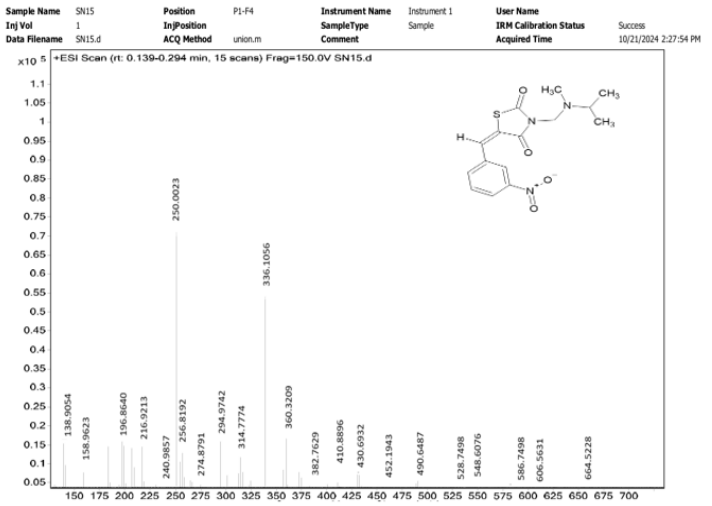
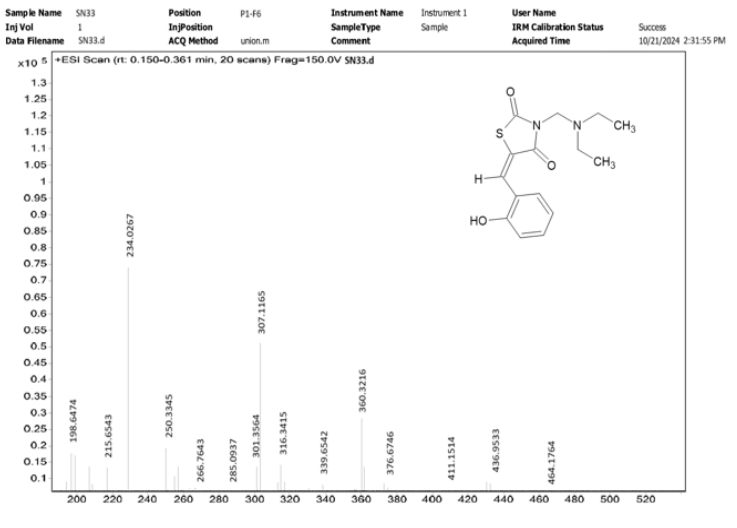
Mass Spectroscopy

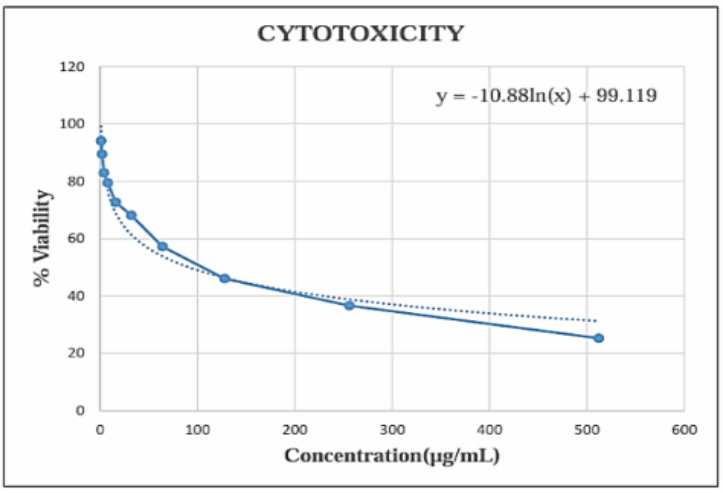
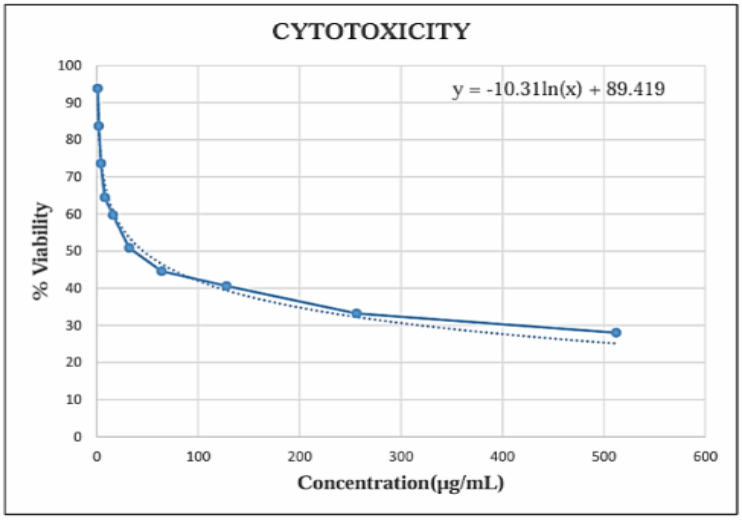
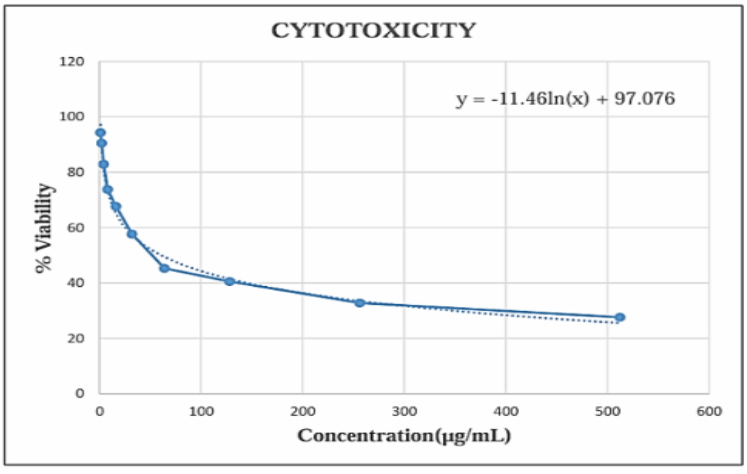
Table 7: Mass spectrum of synthesized compounds.

Compound ID	Mass Spectrum	Molecular weight
SN1C		**321.12 g/mol**
SN15E		**336.10 g/mol**
SN33C		**307.11 g/mol**

***In-Vitro* Studies**

MTT Cytotoxicity Assay (Using HepG2 cell line)

Table 8: IC_{50} value and Concentration Response Curve of synthesized compounds

Compound ID	Concentration (µg/mL) IC_{50} value	Concentration Response Curve
SN1C	**91.342**	
SN15E	**45.758**	
SN33C	**60.816**	

Free Fatty Acid Induction & treatment - Oil Red O Staining

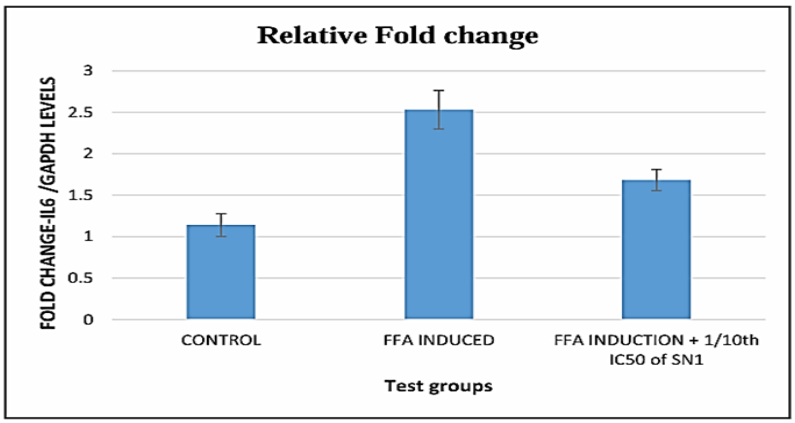
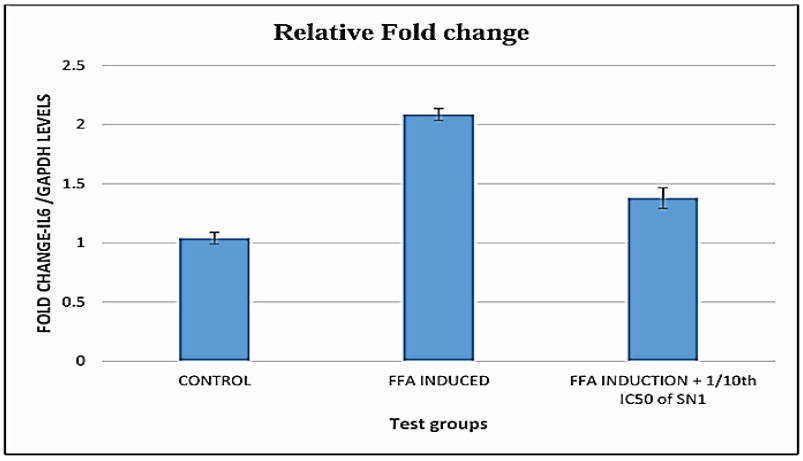
Based on the desired balance between potency and safety, sample SN1C was chosen for further *in-vitro* studies such as Oil Red O Staining and Gene Expression Study.

Figure 5: Oil Red O Staining of Compound SN1C.

Gene Expression Study

Gene expression study was carried out using sample SN1C for TNF-α and IL-6 gene (β-actin - reference gene).

Table 9: Gene Expression Study of Compound SN1C.

Compound ID	SN1C
Gene expression of TNFα	
Gene expression of IL6	

Conclusion

The findings of this research not only highlight the effectiveness of 2,4-thiazolidinedione derivatives in targeting FFAR4 but also pave the way for the development of new pharmacological treatments for NAFLD.

The *in-vitro* evaluation of synthesized compounds demonstrated that:

- SN1C is a promising candidate for NAFLD treatment due to its low toxicity, ability to reduce lipid accumulation (Oil Red O staining), and anti-inflammatory effects (gene expression study), while maintaining cell viability.
- By selecting SN1C based on its safety profile and moderate potency, the study highlights the importance of balancing efficacy and toxicity in developing therapeutics.

Through a comprehensive approach that included *in silico* molecular docking, synthetic chemistry, and *in vitro* biological assays, we successfully identified promising compounds that exhibited significant lipid-lowering activity and favourable safety profiles, underscoring their potential as FFAR4 agonists for NAFLD management.

Our integrated approach—merging computational modelling with synthetic and biological evaluations—provides a robust framework for future drug development in this therapeutic area. Given the increasing prevalence of NAFLD globally, continued exploration of these compounds could play a vital role in addressing this major public health challenge.

Author Contributions

All authors contributed equally to this research. All authors read and approved the final manuscript.

Acknowledgements

We express our sincere thanks to the Department of Pharmaceutical Chemistry, College of pharmacy, Madras Medical College (MMC), Chennai for providing necessary facilities for the research work.

Conflict of Interest

The authors declare no conflict of interest.

Funding

The authors did not receive any fundings from any private or government sources.

Ethical Approvals

This study does not involve experiments on animals or human subjects.

References

1. Seul Ki Han, Soon Koo Baik, and Moon Young Kim. Non-alcoholic fatty liver disease: Definition and subtypes. Clinical and Molecular Hepatology 2023;29 (Suppl): S5-S16.
2. Teng ML, Ng CH, Huang DQ, et al. Global incidence and prevalence of non-alcoholic fatty disease. Clin Mol Hepatol. 2023;29 (Suppl): S32-S42.
3. Lindenmeyer CC, McCullough AJ. The Natural History of Non-alcoholic Fatty Liver Disease-An Evolving View. Clin Liver Dis. 2018;22(1):11-21.
4. Loomba, Rohit et al. Mechanisms and disease consequences of non-alcoholic fatty liver disease. Cell, Volume 184, Issue 10, 2537 - 2564
5. Overview of Non-Alcoholic Fatty Liver Disease (NAFLD) and the Role of Sugary Food Consumption and Other Dietary Components in Its Development. Nutrients. 2021; 13(5):1442.
6. Non-Alcoholic Fatty Liver Disease: Assessment and Management. London: National Institute for Health and Care Excellence (NICE); 2016 (NICE Guideline, No. 49.) 2, https://www.ncbi.nlm.nih.gov/books/NBK384738/
7. Kounatidis D, Vallianou NG, Geladari E, Panoilia MP, Daskou A, Stratigou T, Karampela I, Tsilingiris D, Dalamaga M. NAFLD in the 21st Century: Current Knowledge Regarding Its Pathogenesis, Diagnosis and Therapeutics. Biomedicines. 2024; 12(4):826.
8. Guo X, Yin X, Liu Z, Wang J. Non-Alcoholic Fatty Liver Disease (NAFLD) Pathogenesis and Natural Products for Prevention and Treatment. Int J Mol Sci. 2022;23(24):15489. 2022.
9. Antonella Vetuschi, Roberta Sferra. Simona Pompili. G-Protein-Coupled Receptor 120 Agonist Mitigates Steatotic and Fibrotic Features Triggered in Obese Mice by the Administration of a High-Fat and High-Carbohydrate Diet. ACS Omega 2024, 9, 29, 31899–31909.
10. Tsuru, H., Osaka, M., Hiraoka, Y. et al. HFD-induced hepatic lipid accumulation and inflammation are decreased in Factor D deficient mouse. Sci Rep 10, 17593 (2020).
11. Macalino, S.J.Y., Gosu, V., Hong, S. et al. Role of computer-aided drug design in modern discovery. Arch. Pharm. Res. 38, 1686–1701 (2015).

12. Liu, X., Xue, Z., Luo, M. et al. Anesthetic drug discovery with computer-aided drug design and machine learning. APS 2, 7 (2024).
13. Torres PHM, Sodero ACR, Jofily P, Silva-Jr FP. Key Topics in Molecular Docking for Drug Design. Int J Mol Sci. 2019;20(18):4574. 2019.
14. Abbas Al-Mulla. A Review: Biological Importance of Heterocyclic Compounds. Der Pharma Chemica, 2017, 9(13):141-147.
15. Jampilek J. Heterocycles in Medicinal Chemistry. Molecules. 2019;24(21):3839. Published 2019 Oct 25.
16. Tanzeela Qadir Andleeb Amin PraveenKumar Sharma Ishtiaq Jeelani and Hitoshi Abe. Review on Medicinally Important Heterocyclic Compounds. The Open Medicinal Chemistry Journal,28 2022,
17. Chang E, Park CY, Park SW. Role of thiazolidinediones, insulin sensitizers, in non-alcoholic fatty liver disease. J Diabetes Investig. 2013;4(6):517-524.
18. Wang X, Ji G, Han X, et al. Thiazolidinedione derivatives as novel GPR120 agonists for the treatment of type 2 diabetes. RSC Adv. 2022;12(10):5732-5742. 2022.
19. Ndakotsu A, Vivekanandan G. The Role of Thiazolidinediones in the Amelioration of Nonalcoholic Fatty Liver Disease: A Systematic Review. Cureus. 2022;14(5): e25380. 2022.
20. Prieto-Martinez FD, Lopez-Lopez E, Juarez-Mercado KE, Medina-Franco JL. Computational drug design methods-current and future perspectives. In silico drug design Academic press. 2019; 19-44.
21. Balss B.E. Drug discovery and development: An Overview of Modern Methods and principles. In Basic Principles of Drug discovery and development; Academic Press: Boston. 2015; 1-34.
22. Bhaskar Ankush, Balasaheb Shitole, Nana Shitole. Synthesis of 5-Arylidene-2,4 thiazolidinediones by Knoevenagel Condensation Using Tannic Acid as Catalyst. National Conference on New Trends in Green Chemistry and Environmental Science In Association with International Journal of Scientific Research in Science and Technology Volume 9; Issue 8.
23. Mohammad Shahnaz, Patel Kannu Bhai Ramesh Bhai. Synthesis, Characterization Of 2,4 - Thiazolidinedione Derivatives and Evaluation of Their Antioxidant Activity. Journal Of Drug Delivery & Therapeutics; 2013, 3(6), 96-101 96.
24. Inhye Kim, Mi-lang Kyun, Hyewon Jung, Ji-In Kwon, Jeongha Kim, Ju-Kang Kim, Yu Bin Lee, Young-In Kwon, and Kyoung-Sik Moon. In-Vitro Non-alcoholic Fatty Liver Disease Model Elucidating the Effect of Immune Environment on Disease Progression and Alleviation. ACS Omega 2024 9 (23), 25094-25105.
25. Yong Z, Ruiqi W, Hongji Y, et al. Mangiferin Ameliorates HFD-Induced NAFLD through Regulation of the AMPK and NLRP3 Inflammasome Signal Pathways. J Immunol Res. 2021:4084566.
26. Norberto C Chavez-Tapia, Natalia Rosso and Claudio Tiribelli. Effect of intracellular lipid accumulation in a new model of non-alcoholic fatty liver disease. BMC Gastroenterology 2012, 12:20
27. Lipinski C A, Lombardo F, Dominy B W and Feeney P J. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Advanced Drug Delivery Reviews.2001;46(1-3):3–26.
28. Soret P-A, Magusto J, Housset C, Gautheron J. In-Vitro and In-Vivo Models of Non alcoholic Fatty Liver Disease: A Critical Appraisal. Journal of Clinical Medicine. 2021; 10(1):36.