Synthesis, Spectroscopic Characterization, and In Silico Evaluation of 3-Methyl-6-anilino-1,2,4-triazine as a Promising Antidiabetic Agent

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Abstract- The triazine scaffold remains a cornerstone in the development of biologically active molecules due to its structural versatility and pharmacological potential. In this study, we report the synthesis of 3-methyl-6-anilino-1,2,4-triazine, a brown crystalline compound obtained through the condensation of 3-methyl-6-amino-1,2,4-triazine with aniline hydrochloride. Structural elucidation was carried out via IR, 1H NMR, 13C NMR, and mass spectrometry, confirming the proposed framework. The compound was subjected to SwissADME analysis, which indicated favorable pharmacokinetic properties, high gastrointestinal absorption, and compliance with Lipinski's rule. Molecular docking was performed against PPAR-γ (PDB ID: 3VI8), showing a binding energy of -7.6 kcal/mol and key hydrogen bonding interactions. These findings suggest that the compound could serve as a viable lead for the development of new antidiabetic agents.

Keywords - 1,2,4-triazine, PPAR-γ, molecular docking, antidiabetic, drug-likeness, SwissADME

INTRODUCTION

Diabetes mellitus is a Pandemic disease that has struck each and every corner of the world. According to Indian Council of Medical Research-Indian Diabetes Study (ICMR), a national diabetes study, India Currently has an estimated 77 million people with diabetes, which makes it the second most affected in the world after China. This is set to increase to over 100 million by 2030(1). The Prevalence of diabetes among adults has reached approximately 20% in Urban and approximately 10% in rural populations in India (2). Various classes of antidiabetic drugs including insulin and oral hypoglycemic agents (OHA) are currently used in the treatment of diabetes which acts by different mechanism to reduce blood glucose levels to maintain optimal glycemic control (3,4). The United Kingdom Prospective Diabetes Study showed intensive blood glucose control by either sulfonylureas or insulin substantially decreased the risk of microvascular complications (5,6). The currently used antidiabetic drugs are very effective, however because of lack of patients compliance, clinical inertia, insulin resistance, lack of exercise and lack of dietary control leads to unsatisfactory control of hyperglycemia (7,8,9). In India limited studies have focused on diabetes care and provide an insight into the current profile of patients and their management. More than 50% of people with diabetes have poor glycemic controls, uncontrolled hypertension and large percentage have diabetic vascular complications (10,11). Therefore this study to establish the method of synthesis for proposed new antidiabetic drug supported some Amines, Alkyl, Aryl Alkyl and Triazine Compounds. Diabetes mellitus remains a major global health concern, necessitating the continuous discovery of new and effective therapeutic agents. Among nitrogen-rich heterocycles, triazines, especially the 1,2,4-triazine isomers, have shown promise due to their pharmacophoric characteristics and synthetic modifiability. Building upon these properties, this study explores the synthesis and evaluation of a new triazine derivative: 3-methyl-6-anilino-1,2,4-triazine.

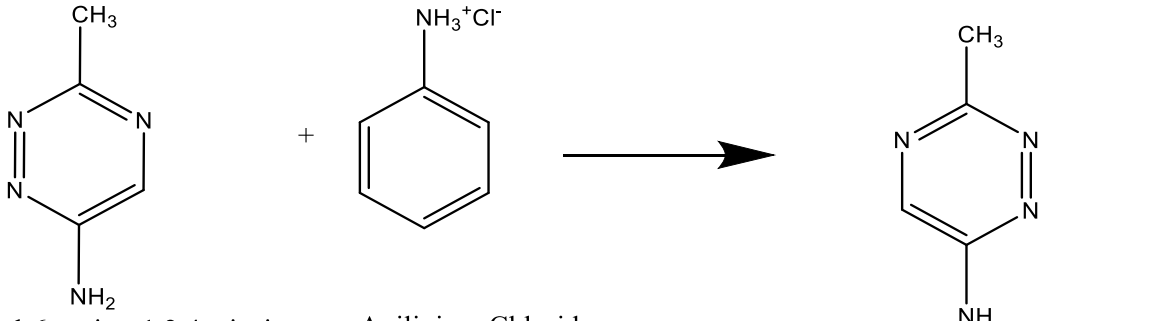
MATERIALS AND METHODS

Firstly Synthesized 3-Methyl 6-Amino-1,2,4-Triazine for further synthesis after that used Aniline which was purchased from Research Lab Fine Chem. And Hydrochloric Acid from ACS Chemicals. The reaction proceeds via nucleophilic aromatic substitution (SNAr).

Synthesis of 3-Methyl-6-anilino-1,2,4-triazine

Firstly Take Round Bottom Flask (RBF) in RBF take 2-3 Porcelain piece and 3-methyl-6-amino-1,2,4-triazine (5gm) dissolve in hot water Start Heating using Sand Bath then Make Anilinium Chloride soln. [take Aniline (5ml) in Test tube then make a Anilinium Chloride Salt using Conc. Hydrochloric Acid (Conc. HCl) (3ml) adding in Aniline Solution]. Then add Slowly Anilinium Chloride salt in Round Bottom Flask (RBF) and Reflux for 2 hours. Then Cool Down Solution at room temperature after that Transfer in ice water. Brown Colour crystals ppts obtain in it. The resulting brown crystalline product was filtered, washed, and dried. Then take a melting point using capillary method. melting point was 250-255^{0}C. Calculate the % of purity of Practical Yield 76.07%.

Scheme



3-methyl-6-amino-1,2,4-triazine Anilinium Chloride 3-methyl-6-anilino-1,2,4-triazine

Thin Layer Chromatography (TLC)

The progress of the reaction and purity of the compound were monitored by thin-layer chromatography (TLC) using silica gel plates. The solvent system used was ethyl acetate: n-hexane (3:1). Visual agent was Iodine Vapours. The Rf value of the purified product was found to be 0.67, confirming its formation and purity.

Characterization Techniques

The synthesized compound was characterized using IR spectroscopy, 1H NMR, 13C NMR, and mass spectrometry. Mass spectra were recorded using an ESI source, IR spectra were recorded using KBr pellets. 1H NMR spectra were obtained in D2O on a 400 MHz spectrometer and 13C NMR spectra were obtained in D2O on a 100 MHz spectrometer.

Spectroscopic Characterization

- Mass Spectrometry (ESI-MS)

m/z 187.1 [M+H]+: Confirms the molecular ion peak corresponding to C10H10N4 (M.W. 186.21 g/mol).

- IR Spectroscopy (KBr, cm^{-1})
- Peaks at 3436 (N-H)
- 3032 (C-H aromatic)
- 1612 (C=N)
- 1504 (C=C aromatic)
- 1254 (C-N)

These peaks confirm the presence of an amino group and triazine ring in the molecule.

- 1H NMR (400 MHz, DMSO-d6, δ ppm)
- δ 2.57 ppm: Singlet, 3H, CH_3
- δ 6.60-7.40 ppm: m, 5H, Ar-H
- δ 5.80 ppm: Singlet,1H, NH
- δ 8.34 ppm: Singlet,1H, NH

The spectrum confirms the expected proton environment with appropriate integration.

- 13C NMR (100 MHz, DMSO-d6, δ ppm)
  - δ 23.8 (1C, s), 119.3 (2C, s), 123.6 (1C, s), 129.3 (2C, s), 141.2 (1C, s), 148.2 (1C, s), 154.0 (1C, s), 164.7 (1C, s).

The number and type of carbon signals match the structure of 3-methyl-6-anilino-1,2,4-triazine.

- The spectral data collectively confirm the structure of the synthesized compound.

SMILES and IUPAC Name
SMILES: CN1CNC(NC1)Nc1ccccc1
IUPAC Name: 3-methyl-6-anilino-1,2,4-triazine

Bioactivity Prediction and Drug-likeness (SwissADME)

- Molecular weight: 186.21 g/mol
- H-bond donors/acceptors: 3/3
- TPSA: 39.33 Å²
- GI absorption: High
- LogP (Consensus): 0.63
- Solubility class: Soluble to very soluble
- Lipinski's rule: 0 violations
- Bioavailability score: 0.55
- No PAINS or Brenk alerts.

Molecular Docking

Docking was carried out using AutoDock Vina targeting PPAR-γ (PDB ID: 3VI8). The ligand exhibited a binding energy of -7.6 kcal/mol and formed stable hydrogen bonds with key amino acid residues including Ser289 and His449, indicating potential antidiabetic activity(17).

RESULTS AND DISCUSSION

Spectral data confirmed the successful synthesis of the desired compound. The IR spectrum confirmed characteristic functional groups. The NMR spectra supported the presence of triazine and aromatic moieties. The mass spectrum corroborated the expected molecular ion peak. SwissADME analysis showed high drug-likeness, solubility, and absorption. Molecular docking showed good binding interactions with the PPAR-γ active site, affirming its antidiabetic potential.

CONCLUSION

A novel triazine derivative, 3-methyl-6-anilino-1,2,4-triazine, was synthesized and fully characterized. It exhibited favorable in silico pharmacokinetics and strong binding to PPAR-γ, supporting its potential as a promising antidiabetic candidate. Further biological assays are warranted to confirm its efficacy.

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