RESEARCH PAPER

Microwave-Assisted Green Synthesis of Chalcone Derivatives with Antidiabetic Potential: In-Vitro Evaluation

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ABSTRACT
The present study focuses on the microwave-assisted green synthesis of chalcone derivatives and their in-vitro antidiabetic evaluation. Chalcones are important intermediates belonging to the flavonoid family and possess a wide range of pharmacological activities including antidiabetic, antioxidant, anti-inflammatory, and antimicrobial properties. Conventional synthesis methods require prolonged reaction time and excessive solvent consumption, whereas microwave-assisted synthesis offers rapid reaction rates, improved yield, and environmentally friendly processing.
In this work, various chalcone derivatives were synthesized through Claisen–Schmidt condensation between substituted acetophenones and aromatic aldehydes using ethanol as a green solvent and sodium hydroxide as catalyst under microwave irradiation. The synthesized compounds were characterized using melting point determination, Thin Layer Chromatography (TLC), Fourier Transform Infrared Spectroscopy (FTIR), Nuclear Magnetic Resonance (1H-NMR), and Mass Spectroscopy.
The synthesized chalcone derivatives were evaluated for in-vitro antidiabetic activity using α-amylase and α-glucosidase inhibition assays. Several derivatives demonstrated significant enzyme inhibitory activity when compared with the standard drug acarbose. The study concludes that microwave-assisted green synthesis is an efficient and eco-friendly approach for developing chalcone derivatives with promising antidiabetic potential.
Keywords: *Chalcone derivatives, Microwave-assisted synthesis, Green chemistry, Antidiabetic activity, α-amylase inhibition, α-glucosidase inhibition.*
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1. INTRODUCTION

Diabetes mellitus is one of the most common chronic metabolic disorders characterized by elevated blood glucose levels due to defects in insulin secretion, insulin action, or both. According to the International Diabetes Federation (IDF), the prevalence of diabetes is increasing rapidly worldwide and poses a major public health challenge. Long-term complications of diabetes include cardiovascular disease, nephropathy, neuropathy, and retinopathy.(1-3)

Current antidiabetic therapies are associated with various adverse effects such as hypoglycemia, gastrointestinal disturbances, and weight gain. Therefore, there is a continuous demand for the development of novel therapeutic agents with improved efficacy and safety.

Chalcones are open-chain flavonoids containing two aromatic rings connected by a three-carbon α,β-unsaturated carbonyl system. These compounds exhibit diverse biological activities including antidiabetic, antioxidant, anticancer, antimicrobial, anti-inflammatory, and antihypertensive activities. The presence of reactive enone functionality contributes significantly to their pharmacological properties.(4-5)

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Microwave-assisted organic synthesis has emerged as an important green chemistry technique due to its advantages such as reduced reaction time, improved product yield, energy efficiency, and reduced solvent usage. Microwave irradiation accelerates chemical reactions by direct interaction with polar molecules and ionic species.

The present study aims to synthesize chalcone derivatives using a microwave-assisted green chemistry approach and evaluate their in-vitro antidiabetic activity using enzyme inhibition assays.(6-7)

2. OBJECTIVES OF THE STUDY

1. To synthesize chalcone derivatives using microwave-assisted synthesis.
2. To employ green chemistry principles for eco-friendly synthesis.
3. To characterize synthesized compounds using spectroscopic techniques.
4. To evaluate in-vitro antidiabetic activity using α-amylase inhibition assay.
5. To evaluate in-vitro antidiabetic activity using α-glucosidase inhibition assay.
6. To compare the activity of synthesized compounds with standard antidiabetic drugs.

3. MATERIALS AND METHODS

3.1 Materials

The chemicals used in the study included substituted acetophenones, aromatic aldehydes, ethanol, sodium hydroxide, dimethyl sulfoxide (DMSO), starch solution, α-amylase enzyme, α-glucosidase enzyme, p-nitrophenyl-α-D-glucopyranoside, and acarbose.

All chemicals and reagents used were of analytical grade.

3.2 Instruments Used

- Microwave synthesizer
- Digital melting point apparatus
- UV chamber
- FTIR spectrophotometer
- Nuclear Magnetic Resonance (NMR) spectrometer
- Mass spectrometer
- UV-Visible spectrophotometer

3.3 General Procedure for Microwave-Assisted Synthesis of Chalcone Derivatives (7-9)

Equimolar quantities of substituted acetophenone and substituted aromatic aldehyde were dissolved in ethanol. Sodium hydroxide solution was added slowly with continuous stirring. The reaction mixture was subjected to microwave irradiation at controlled power for 2–5 minutes.

The completion of the reaction was monitored using Thin Layer Chromatography (TLC). After completion, the reaction mixture was poured into ice-cold water and acidified using dilute hydrochloric acid. The precipitated chalcone derivative was filtered, washed with distilled water, dried, and recrystallized from ethanol.

General Reaction Scheme (10-11)

Substituted Acetophenone + Aromatic Aldehyde → Chalcone Derivative

(Claisen–Schmidt condensation under microwave irradiation)

3.4 Characterization of Synthesized Compounds

3.4.1 Melting Point Determination

The melting points of synthesized compounds were determined using a digital melting point apparatus and were found to be uncorrected.

3.4.2 Thin Layer Chromatography (TLC)

TLC was performed using silica gel-coated plates with suitable mobile phase systems. Spots were visualized under UV light.

3.4.3 FTIR Spectroscopy

FTIR spectra were recorded to identify characteristic functional groups such as carbonyl (C=O), aromatic C=C, and methoxy or hydroxyl substitutions.

3.4.4 NMR Spectroscopy

1H-NMR spectroscopy was carried out to confirm the chemical structure of synthesized chalcone derivatives.

3.4.5 Mass Spectroscopy

Mass spectral analysis was performed to determine molecular weight and fragmentation pattern. **4. In-Vitro Antidiabetic Evaluation (12-15)**

4.1 α-Amylase Inhibition Assay

Principle

The α-amylase inhibition assay is based on the ability of compounds to inhibit the breakdown of starch into simple sugars by the α-amylase enzyme.

Procedure

1. Different concentrations of synthesized compounds were prepared.
2. α-Amylase enzyme solution was added to each test tube.
3. The mixture was incubated at 37°C for 10 minutes.
4. Starch solution was added and incubated further.
5. DNS reagent was added and heated.
6. Absorbance was measured at 540 nm using a UV spectrophotometer.

Formula

$$\% \text{ Inhibition} = [(Ac - As) / Ac] \times 100$$

Where:

- Ac = Absorbance of control

- As = Absorbance of sample

4.2 α-Glucosidase Inhibition Assay (16-20)

Principle
The assay measures the inhibition of α-glucosidase enzyme responsible for carbohydrate digestion.

Procedure
1. Test samples of different concentrations were prepared.
2. α-Glucosidase enzyme was added.
3. The reaction mixture was incubated.
4. p-Nitrophenyl-α-D-glucopyranoside substrate was added.
5. Absorbance was measured at 405 nm.

Formula
% Inhibition = [(Ac − As) / Ac] × 100

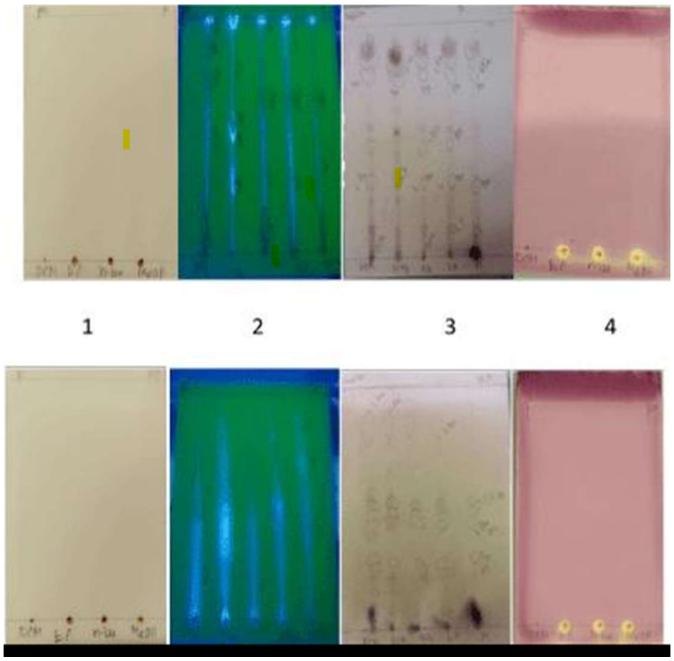
5. RESULTS AND DISCUSSION

5.1 Synthesis of Chalcone Derivatives
Microwave-assisted synthesis produced chalcone derivatives in excellent yields within a short reaction time compared to conventional heating methods. The use of ethanol as a green solvent reduced environmental hazards and improved sustainability.

The synthesized compounds were obtained in yields ranging from 78% to 92%. The reaction time was significantly reduced from several hours to a few minutes.

5.2 Characterization Results

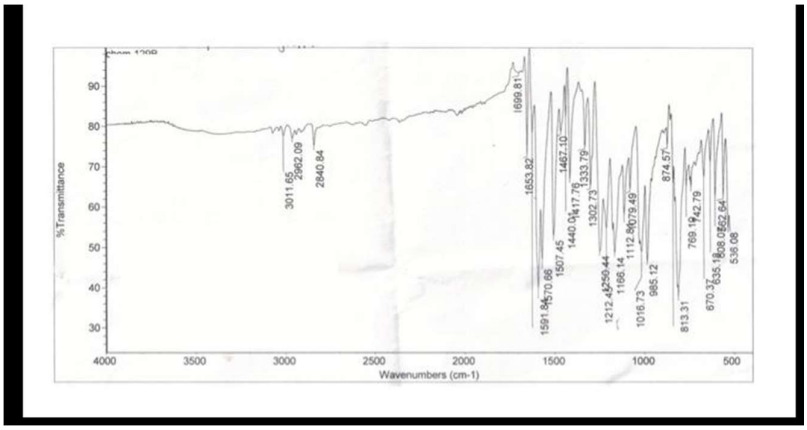
TLC Analysis-



Compound	Solvent System	Rf Value
CH-1	Hexane:Ethyl acetate (8:2)	0.54
CH-2	Hexane:Ethyl acetate (7:3)	0.61
CH-3	Hexane:Ethyl acetate (7:3)	0.65
CH-4	Hexane:Ethyl acetate (6:4)	0.72

Single spots were observed indicating purity of synthesized chalcone derivatives.

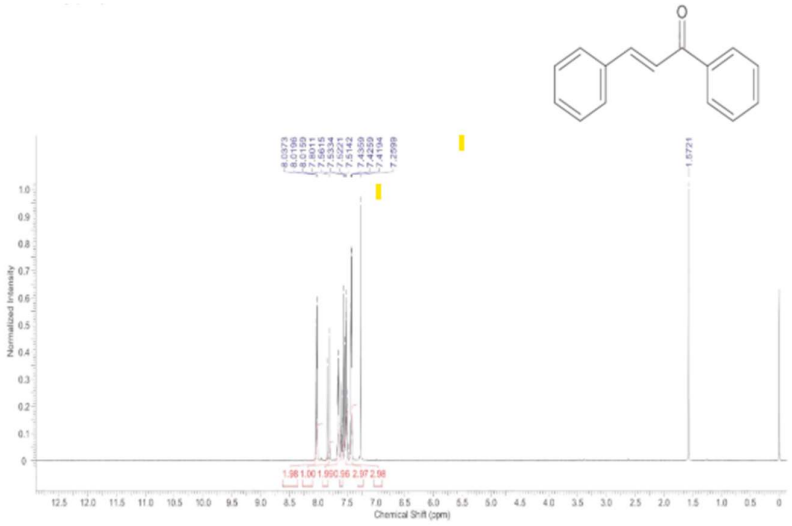
IR Spectra–



The synthesized compounds showed characteristic FTIR peaks around:

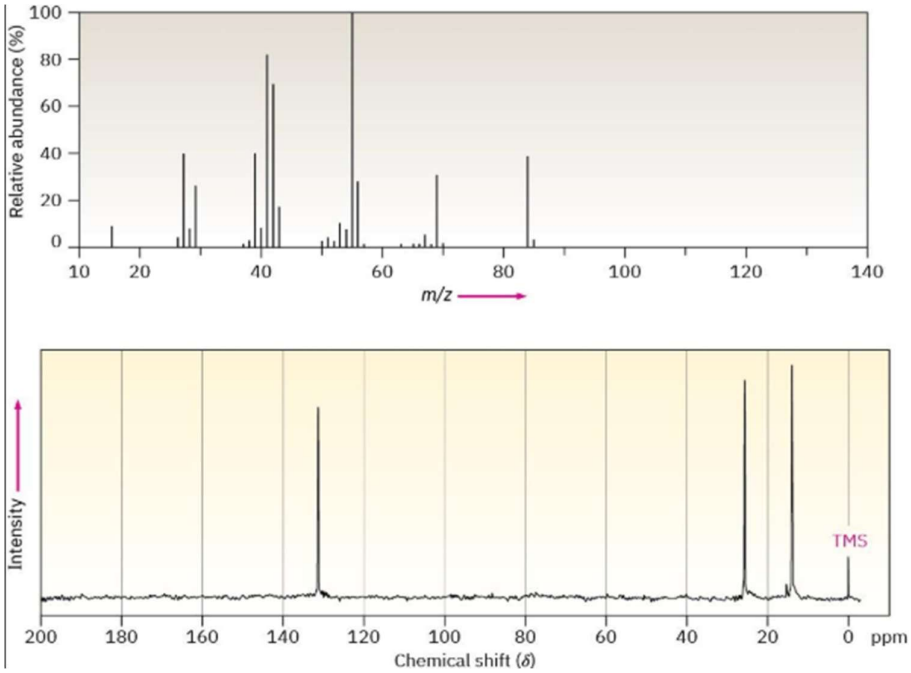
- 1650–1680 cm−1 for carbonyl group (C=O)
- 1500–1600 cm−1 for aromatic C=C stretching
- 3000–3200 cm−1 for hydroxyl group

NMR spectra-



NMR spectra confirmed the presence of aromatic protons and α,β-unsaturated carbonyl moiety.

Mass spectra-



Mass spectra confirmed the molecular weight of synthesized compounds.

5.3 In-Vitro Antidiabetic Activity

Several synthesized chalcone derivatives demonstrated promising α-amylase and α-glucosidase inhibitory activity.

Activity Table

Compound Code	% α-Amylase Inhibition	% α-Glucosidase Inhibition
CH-1	62.4 ± 0.5	58.7 ± 0.3
CH-2	70.2 ± 0.4	66.1 ± 0.5
CH-3	74.8 ± 0.6	71.5 ± 0.4
CH-4	81.3 ± 0.2	76.4 ± 0.3
Acarbose	88.5 ± 0.3	84.2 ± 0.4

The results indicated that electron-donating substituents such as hydroxyl and methoxy groups enhanced antidiabetic activity.

Microwave-assisted synthesis provided higher purity compounds and better yields than conventional synthesis techniques.

6. ADVANTAGES OF MICROWAVE-ASSISTED GREEN SYNTHESIS

1. Reduced reaction time
2. Higher reaction yield
3. Eco-friendly approach
4. Lower energy consumption
5. Reduced solvent usage
6. Better purity of products
7. Simplified work-up procedure

7. CONCLUSION

The present study successfully demonstrated the microwave-assisted green synthesis of chalcone derivatives using environmentally friendly conditions. The synthesized compounds were characterized by various spectroscopic methods and evaluated for in-vitro antidiabetic activity.

Several chalcone derivatives exhibited significant α-amylase and α-glucosidase inhibitory activity, suggesting their potential as promising antidiabetic agents. Microwave-assisted synthesis proved to be an efficient, rapid, and sustainable method for the preparation of bioactive chalcone derivatives.

Further studies including in-vivo evaluation, toxicity studies, and molecular docking investigations are recommended to establish the therapeutic potential of these compounds.

8. FUTURE SCOPE

1. Molecular docking studies against diabetic targets.
2. In-vivo antidiabetic studies in animal models.
3. Pharmacokinetic and toxicity studies.
4. Structural optimization of chalcone derivatives.
5. Development of novel chalcone-based formulations.

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