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# Synthesis, Spectral Characterization, and Biological Evaluation of a Novel Curcumin–L-Cystine Schiff Base Derivative

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**Abstract:**

Curcumin, a natural polyphenolic compound derived from Curcuma longa, possesses diverse biological activities including antimicrobial and antioxidant effects. However, its clinical application is limited by poor aqueous solubility and low bioavailability [1–5]. In this study, a novel curcumin–L-cystine Schiff base derivative was synthesized via condensation under reflux conditions with a yield of 74%. The structure was confirmed using FT-IR, $^{1}$H-NMR, and $^{13}$C-NMR spectroscopy. Antibacterial activity was evaluated against Gram-negative (Escherichia coli, Klebsiella pneumoniae) and Gram-positive (Staphylococcus aureus, Staphylococcus agalactiae) strains using the agar well diffusion method [19]. Antioxidant activity was assessed via the DPPH radical scavenging assay [10,11]. The derivative exhibited concentration-dependent moderate antibacterial activity, particularly against Gram-positive bacteria, while antioxidant activity was lower than that of ascorbic acid. These findings demonstrate that amino acid conjugation via Schiff base formation modifies curcumin's biological profile and may serve as a promising strategy for further structural optimization.

**Keywords**: Curcumin; L-Cystine; Schiff Base; Antibacterial Activity; Antioxidant Activity; Spectral Characterization.

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# تخليق،وتوصيف طيفي،وتقييم بيولوجي لمشتق جديدمن قاعدة شيف للكركمين مع L- سيستين

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**الملخص:**

يُعدّ الكركمين مركبًا بوليفينوليًا طبيعيًا مستخلصًا من نبات الكركم (Curcuma longa)، ويتميز بامتلاكه أنشطة بيولوجية متعددة تشمل التأثيرات المضادة للبكتيريا والمضادة للأكسدة. إلا أن استخدامه السريري يظل محدودًا بسبب ضعف ذوبانه في الماء، وسرعة استقلابه، وانخفاض توافره الحيوي. في هذه الدراسة، تم تحضير مشتق جديد من قاعدة شيف للكركمين مع L-سيستين عن طريق تفاعل تكاثف تحت ظروف الارتجاع، بنسبة حصيلة بلغت 74%. تم تأكيد البنية التركيبية للمركب باستخدام تقنيات الأشعة تحت الحمراء (FT-IR)، والرنين المغناطيسي النووي للبروتون ($H-NMR^1$)، والكربون ($C-NMR^{13}$).

تم تقييم النشاط المضاد للبكتيريا ضد سلالات سالبة الجرام (Escherichia coli و Klebsiella pneumoniae) وموجبة الجرام (Staphylococcus aureus و Staphylococcus agalactiae) باستخدام طريقة الانتشار في حفر الآجار. كما تم تقييم النشاط المضاد للأكسدة باستخدام اختبار اصطياد الجذور الحرة (DPPH). أظهر المشتق نشاطًا مضادًا للبكتيريا يعتمد على التركيز، وكان أكثر فاعلية ضد البكتيريا موجبة الجرام، في حين كان نشاطه المضاد للأكسدة أقل مقارنة بحمض الأسكوربيك. وتشير هذه النتائج إلى أن اقتران الأحماض الأمينية عبر تكوين قاعدة شيف يؤدي إلى تعديل الخصائص البيولوجية للكركمين، مما يجعله نهجًا واعدًا لمزيد من التحسين البنيوي مستقبلاً

**الكلمات المفتاحية:** الكركمين؛L-Cystine ؛ قاعدة شيف؛ الفعالية المضادة للبكتيريا؛ النشاط المضاد للأكسدة؛ التوصيف الطيفي.

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## Introduction

Curcumin is the principal bioactive constituent of Curcuma longa and has been extensively investigated for its antimicrobial, antioxidant, anti-inflammatory, and anticancer activities [1–4,16,17]. Its biological activity arises primarily from phenolic hydroxyl groups and a conjugated β-diketone system [2,6]. Despite promising pharmacological potential, curcumin suffers from poor water solubility, rapid

group, which has been associated with enhanced antimicrobial properties [7–9]. Conjugation with amino acids such as L-cystine may improve physicochemical properties and introduce redox-active disulfide functionality [15].

Given the increasing challenge of antimicrobial resistance [14], the development of novel curcumin derivatives represents an important strategy for designing improved bioactive compounds. Therefore, the present study focuses on the synthesis, spectral characterization, and biological evaluation of a novel curcumin–L-cystine Schiff base derivative.

## Material and methods

### Chemicals

Curcumin, L-cystine, sodium acetate, glacial acetic acid, and ammonium hydroxide were of analytical grade.

### Synthesis of Curcumin–L-Cystine Schiff Base

Curcumin (1.5 mmol, 0.5 g) was dissolved in glacial acetic acid (8 mL). L-cystine (0.24 g) and sodium acetate (1.5 mmol, 0.2 g) were added. The mixture was refluxed for 14 h. After cooling, the reaction mixture was neutralized with ammonium hydroxide to afford a dark brown precipitate. The product was filtered, washed, and recrystallized.

Yield: 0.626 g (74%)

Melting point: 89–90 °C

The relatively low melting point compared to native curcumin (≈183 °C) may be attributed to altered molecular packing and increased structural flexibility induced by Schiff base formation and the disulfide linkage.

### Proposed Reaction Mechanism

The reaction is proposed to occur at one of the carbonyl groups within the β-diketone moiety of curcumin. The primary amine (–$NH_2$) group of L-cystine nucleophilically

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attacks the carbonyl carbon, forming a carbinolamine intermediate. Subsequent dehydration leads to the formation of the azomethine (C=N) linkage characteristic of Schiff bases [7,8].

**Scheme 1. Synthetic route of the curcumin–L-cystine Schiff base derivative.**

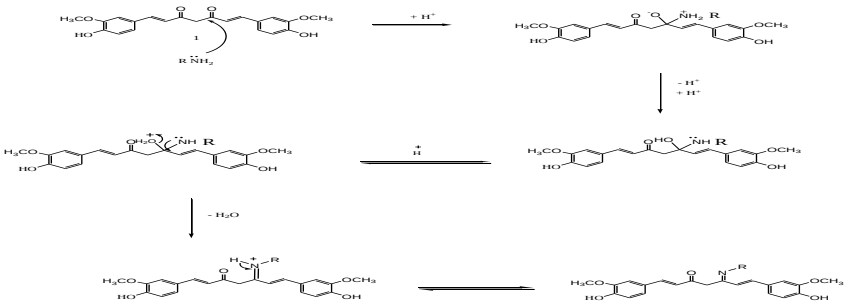
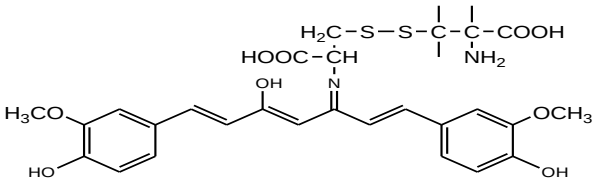


**Figure 1. Chemical structure of the synthesized derivative.**



**Antibacterial Activity**

Tested against Gram-negative (E. coli, K. pneumoniae) and Gram-positive (S. aureus, S. agalactiae) using agar well diffusion. Evaluated at 100, 200, and 300 ppm.

**Antioxidant Activity**

Assessed using DPPH radical scavenging assay at 517 nm.

**Results and discussion**

**Spectral Analysis**

FT-IR Analysis

The FT-IR spectrum showed a characteristic C=N stretching band at 1558 $cm^{-1}$, confirming Schiff base formation. The phenolic O–H stretching band at 3331 $cm^{-1}$ indicated retention of hydroxyl groups. Other peaks corresponded to aromatic C=C and C–O stretching vibrations.

.H-NMR and $^{13}$C-NMR

The $^{1}$H-NMR spectrum (DMSO-$d_6$) displayed signals consistent with aromatic protons and the azomethine proton. The $^{13}$C-NMR spectrum confirmed the presence of imine carbon and aromatic carbons, supporting successful condensation [6].

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**Figure 2. FT-IR spectrum of the derivative.**

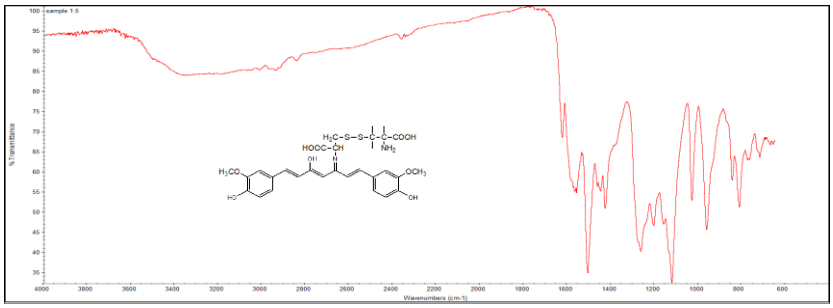


**Figure 3. $^{1}$H-NMR spectrum (DMSO-d$_6$)**

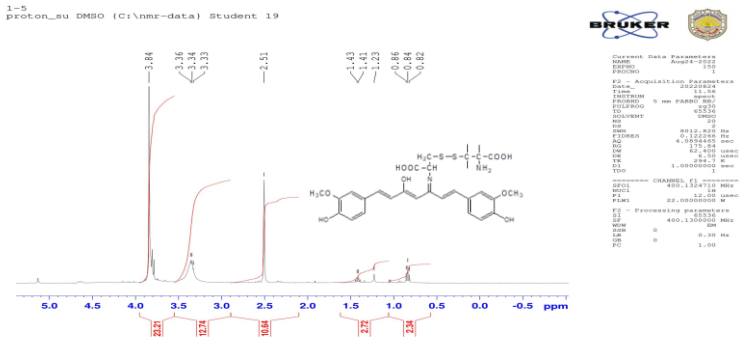
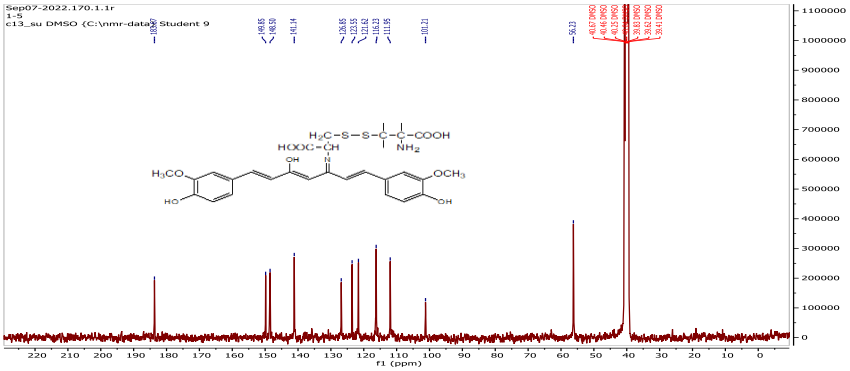


**Figure 4. $^{13}$C-NMR spectrum (DMSO-d$_6$)**



**Antibacterial Activity**

Antibacterial activity was evaluated against Gram-negative (E. coli, K. pneumoniae) and Gram-positive (S. aureus, S. agalactiae) strains using the agar well diffusion method [19].

**Results:**

100ppm → no inhibition

200ppm → 11 mm inhibition against S. aureus

300ppm → 12 mm inhibition against S. aureus and K. pneumoniae

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The derivative exhibited concentration-dependent activity. Gram-positive bacteria were more susceptible, possibly due to the absence of an outer membrane barrier [13]. Compared to standard antibiotics such as gentamicin (20–25 mm inhibition zones), the compound demonstrated moderate antibacterial activity [12].

The presence of azomethine (C=N) and disulfide (–S–S–) groups may enhance interaction with microbial cellular components.

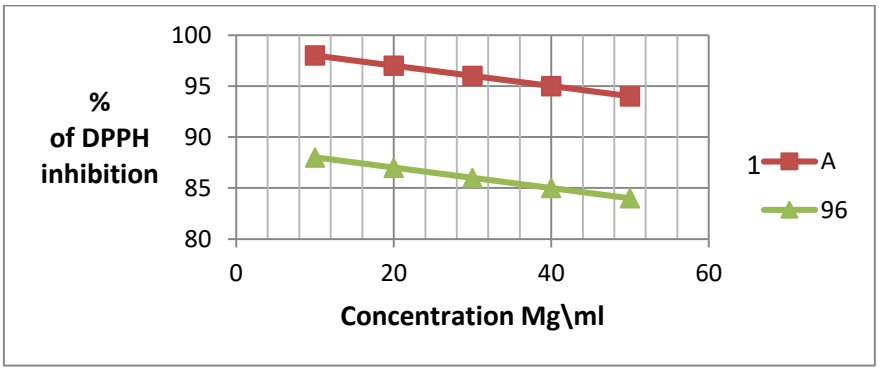
**Antioxidant Activity**

Antioxidant activity was determined using the DPPH radical scavenging assay at 517 nm [10,11]. The derivative exhibited lower radical scavenging activity compared to ascorbic acid. The higher $IC_{50}$ value indicates reduced antioxidant efficiency, possibly due to partial involvement of phenolic hydroxyl groups in Schiff base formation and decreased solubility.

**Discussion**

Conjugation of curcumin with L-cystine significantly modifies its biological behavior. Schiff base formation enhances antibacterial activity, particularly against Gram-positive strains, while slightly reducing antioxidant potential. These findings support amino acid conjugation as a promising approach for structural tuning of curcumin derivatives**.**

**Figure 5. DPPH radical scavenging activity of the derivative.**




**Conclusion**

A novel curcumin–L-cystine Schiff base derivative was successfully synthesized and characterized spectroscopically. The compound exhibited moderate concentration-dependent antibacterial activity, particularly against Gram-positive bacteria, and lower antioxidant activity compared to ascorbic acid. Further structural optimization may enhance its pharmacological potential.

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