



SUSTAINABLE SYNTHESIS OF INDENE-1,3(2H)-DIONE DERIVATIVES USING KINNOW PEEL POWDER AS A RENEWABLE CATALYST

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Abstract

This study presents an efficient and environmentally sustainable approach for synthesizing a novel series of indene-1,3(2H)-dione derivatives **3a-f** via the condensation of ninhydrin (**1**) with various aromatic amines (**2a-f**), including aniline, 4-nitroaniline, p-Toluidine, 4-Acetyl aniline, 4-Methoxy aniline, and 1-naphthylamine. The reaction is facilitated by Kinnow peel powder, a green and renewable catalyst, and proceeds under mild conditions (room temperature with stirring). Kinnow peel powder serves as a catalyst, highlighting the eco-friendly nature of the process and aligning with the principles of green chemistry by minimizing environmental impact and promoting sustainability. In addition to the synthesis, the antifungal activity of all synthesized compounds **3a-f** was evaluated using Mycosal as a reference drug. The results revealed that most of the compounds exhibited promising antifungal activity against *S. cerevisiae* and *Candida*, demonstrating their potential as effective antifungal agents.

Keywords: Synthesis, green chemistry, antifungal, Kinnow peel powder, catalyst.

Introduction

The development of sustainable and environmentally benign synthetic methodologies has become a cornerstone of modern organic chemistry, driven by the increasing demand for green and eco-friendly processes [I]. In recent years, the principles of **green chemistry** have gained significant attention, emphasizing the need to minimize waste, reduce the use of hazardous chemicals, and employ renewable resources in chemical synthesis [Ii]. Green chemistry aims to design chemical processes that are inherently safer for the environment and human health while maintaining efficiency and cost-effectiveness [Iii]. Among the various strategies to achieve these goals, the use of **biomass-derived catalysts** has emerged as a promising approach, offering both ecological and economic advantages [Iv].

Indene-1,3(2H)-dione derivatives are a class of compounds with significant biological and pharmaceutical importance. These compounds exhibit a wide range of biological activities,

including antimicrobial, antioxidant, anti-inflammatory, and anticancer properties [V]. Their versatile pharmacological profile makes them valuable intermediates in the synthesis of various heterocyclic compounds, which are often used in drug discovery and development [VI]. However, traditional methods for synthesizing these derivatives typically involve harsh reaction conditions, toxic catalysts, and environmentally harmful solvents, which contradict the principles of green chemistry [VII]. Therefore, there is a growing need to develop alternative synthetic routes that are both efficient and environmentally sustainable, aligning with the 12 principles of green chemistry, such as the use of renewable feedstocks, waste prevention, and energy efficiency [VIII].

In this study, we present a novel and eco-friendly approach for the synthesis of indene-1,3(2H)-dione derivatives via the Schiff base reaction, utilizing Kinnow peel powder as a green catalyst [IX]. Kinnow, a citrus fruit widely cultivated in regions such as South Asia, produces a significant amount of peel as agricultural waste [X]. Traditionally, this peel is discarded, contributing to environmental waste management challenges [XI]. However, the Kinnow peel is rich in bioactive compounds, including polyphenols, flavonoids, and organic acids, which possess inherent catalytic properties [XII]. By repurposing Kinnow peel powder as a catalyst, we not only provide a sustainable solution to agricultural waste management but also introduce a cost-effective and renewable catalytic system for organic synthesis [XIII]. This approach exemplifies the principles of green chemistry by utilizing a renewable resource, reducing the need for toxic chemicals, and operating under mild reaction conditions [XIV].

The proposed method involves the condensation of ninhydrin with various aromatic amines under mild conditions (room temperature with stirring), facilitated by Kinnow peel powder [XV]. The catalytic activity of Kinnow peel powder is attributed to its natural acidic and functional groups, which promote the Schiff base reaction efficiently [XVI]. This approach aligns with the principles of green chemistry by avoiding toxic reagents, reducing energy consumption, and utilizing a renewable resource [XVII]. The use of Kinnow peel powder as a catalyst highlights the potential of biomass-derived materials in promoting sustainable chemical processes, offering a viable alternative to conventional synthetic methods [XVIII].

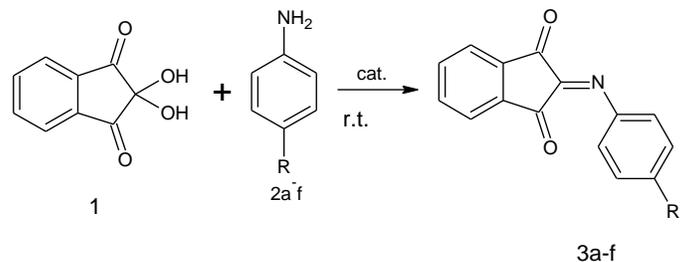
This study aims to demonstrate the efficacy of Kinnow peel powder as a green catalyst, paving the way for its application in the synthesis of other valuable organic compounds [XIX]. By integrating sustainability with synthetic efficiency, this work contributes to the ongoing efforts to develop greener and more sustainable chemical processes while also providing access to biologically active indene-1,3(2H)-dione derivatives with potential pharmaceutical applications [XX]. The adoption of such green methodologies not only reduces the environmental footprint of chemical synthesis but also supports the global transition toward sustainable and eco-friendly industrial practices [XXI].

Results and Discussion

The synthesis of indene-1,3(2H)-dione derivatives **3a-f** (Scheme 1) was successfully achieved through the Schiff base reaction between ninhydrin and various aromatic amines, including aniline, 4-nitroaniline, p-Toludine, 4-Acetyl aniline, 4-Methoxy aniline, and 1-naphthylamine, in the presence of 10 mg of Kinnow peel powder as a green catalyst [XIX]. The reaction proceeded under mild conditions (room temperature with stirring), yielding products in good to excellent yields, ranging from 75% to 92%. The use of Kinnow peel powder as a catalyst not only facilitated the reaction but also eliminated the need for toxic reagents and harsh reaction conditions, aligning with the principles of green chemistry.

The reaction progress was monitored using thin-layer chromatography (TLC), and the products were characterized by spectroscopic techniques, including UV and IR spectra. The IR spectra of

the synthesized compounds showed characteristic peaks corresponding to the C=O stretching vibrations in the range of 1689–1674 cm^{-1} , as well as the C=N stretching vibrations of the Schiff base linkage at 1610–1617 cm^{-1} .



2,3a,R=H
 b,R=4-NO₂
 c,R=CH₃
 d,R=CH₃CO
 e,R=OCH₃
 f,R=Ph

Scheme 1: synthesis of indene-1,3(2H)-dione derivatives **4a-f**

Antimicrobial activity

The antifungal activity of the synthesized compounds was evaluated against *Aspergillus flavus* and *Candida albicans* using the standard antifungal agent mycosal. The results of the antifungal screening are summarized in Table 1, and it shows that the derivatives **3b** and **3d** exhibited higher antifungal activity towards *A. flavus* and *C. albicans* (ZI = 4-8 mm) than mycosal (ZI = 1-2 mm). Moreover, compounds **3c** and **3e** exhibited antifungal activity against *C. albicans* and *A. flavus*. Finally, **3a** and **3f** did not record any antifungal activity.

Table 1. Antimicrobial evaluation of the synthesized compounds **3a-f**.

Compound No.	Fungi	
	<i>Aspergillus flavus</i>	<i>Candida albicans</i>
Inhibition zone diameter (mm/mg sample) (n=3)		
Mycosal	2	1
3a	0	0
3b	4	5
3c	2	3
3d	6	8
3e	2	3
3f	0	0
Control DMSO	0	0

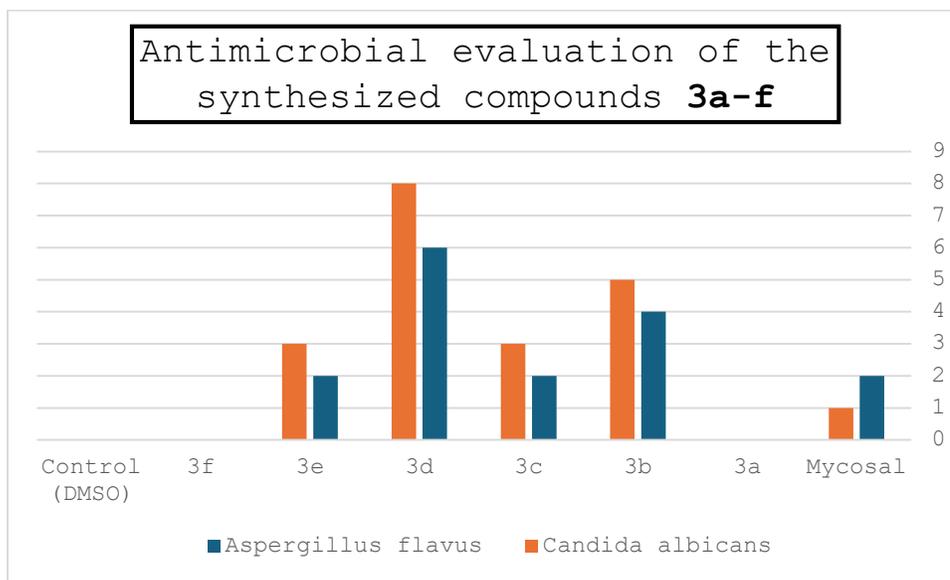


Figure 1: Antimicrobial evaluation of the synthesized compounds 3a-f

Materials. Waste peels of Kinnow mandarin were selected and used as a catalyst for this study. Kinnow peels are collected from the market in Sakaka, Al Jouf, Saudi Arabia. Bruker Fourier transform infrared spectroscopy (FT-IR) and thin layer chromatography (TLC) are performed to characterize the Kinnow peel powder.

Preparation of the catalyst. Kinnow peel waste is washed with deionized water to remove dirt particles and cleaned thoroughly. The peel is dried in an oven for 24 h at 70 °C to remove the moisture content. The dried peel waste is converted into powder form, and then the powder is stored for further experimentation. [XXII]

Preparation of Schiff base and its derivatives. 10 mg of Kinnow peel powder is added to the reaction mixture of 1 mmol of ninhydrin and 1 mmol of Aniline derivatives in a test tube, and it is stirred for 3 minutes on the magnetic stirrer at room temperature. The performance of the reaction is checked by TLC, and after the completion of the catalytic reaction, the desired product is recrystallized in ethanol.

2 -(phenylimino) -1H-indene-1,3(2H) -dione (3a)

80% yield as deep orange Crystals; mp 170-172 °C; U.V (λ_{max}) 318, 425 nm; IR (KBr): ν (cm⁻¹), 1689–1674 cm⁻¹ (C=O), 1610–1617 cm⁻¹ (C=N) ; Anal Calcd for : C₁₅H₉NO₂(235.24): Calcd; C, 76.59; H, 3.86; N, 5.95; Found: C, 76.62; H, 3.89; N, 5.99.

2 -((4-nitrophenyl) imino)-1H-indene-1,3(2H)-dione(3b)

75% yield as yellowish green Crystals; mp 185-187 °C; U.V (λ_{max}) 320, 417 nm; IR (KBr): ν (cm⁻¹), 1689–1674 cm⁻¹ (C=O), 1610–1617 cm⁻¹ (C=N) ; Anal Calcd for C₁₅H₈N₂O₄(280.24): Calcd; C, 64.29; H, 2.88; N, 10.00; Found: C, 64.32; H, 2.93; N, 10.05 .

(p-tolylimino) -1H-indene-1,3(2H) -dione(3c)

88% yield as Orange Crystals; mp 190-192 °C; U.V (λ_{max}) 318, 420 nm; IR (KBr): ν (cm⁻¹), 1689–1674 cm⁻¹ (C=O), 1610–1617 cm⁻¹ (C=N) ; Anal Calcd for C₁₆H₁₁NO₂(: 249.27): Calcd; C, 77.10; H, 4.45; N, 5.62; Found ;C, 77.14; H, 4.49; N, 5.65.

2-((4-acetylphenyl) imino)-1H-indene-1,3(2H)-dione (3d)

87% yield as green Crystals; mp 180-182 °C; U.V (λ_{max}) 315, 425 nm; IR (KBr): ν (cm⁻¹), 1689–1674 cm⁻¹ (C=O), 1610–1617 cm⁻¹ (C=N) ; Anal Calcd for C₁₇H₁₁NO₃(277.28): Calcd: C, 73.64; H, 4.00; N, 5.05; Found ; C, 73.66; H, 4.04; N, 5.08.

2-((4-methoxyphenyl) imino)-1H-indene-1,3(2H)-dione(3e)

92% yield as white, green Crystals; mp 196-198 °C; U.V (λ_{max}) 321, 423 nm; IR (KBr): ν (cm⁻¹), 1689–1674 cm⁻¹ (C=O), 1610–1617 cm⁻¹ (C=N) ; Anal Calcd for C₁₆H₁₁NO₃(265.27): Calcd; C, 72.45; H, 4.18; N, 5.28; Found; C, 74.45; H, 4.22; N, 5.31.

2-(naphthalen-1-ylimino)-1H-indene-1,3(2H)-dione(3f)

79% yield as yellow Crystals; mp 188-190 °C; U.V (λ_{max}) 326, 433 nm; IR (KBr): ν (cm⁻¹), 1689–1674 cm⁻¹ (C=O), 1610–1617 cm⁻¹ (C=N) ; Anal Calcd for C₁₉H₁₁NO₂(285.30): Calcd; C, 79.99; H, 3.89; N, 4.91; Found;; C, 80.01; H, 3.91; N, 4.93.

Biological activity (Sensitivity tests) by Kirby-Bauer Method

The antimicrobial activity of the tested samples was determined using a modified Kirby–Bauer disk diffusion method [XXIII]. Briefly, 100 μ L of the test bacteria/fungi grew in 10 mL of fresh media until they reached a count of approximately 10⁵ cells/mL for fungi [XXIII]. One hundred microliters of a microbial suspension were spread onto agar plates corresponding to the broth in which they were maintained. Isolated colonies of each organism that might be playing a pathogenic role should be selected from primary agar plates and tested for susceptibility by the disk diffusion method. [XXIV, XXV] Many media are available, but NCCL recommends Mueller–Hinton agar due to its results in good batch-to-batch reproducibility. Disk diffusion method for filamentous fungi tested using the approved standard method (M38-A) developed by the for evaluating the susceptibility of filamentous fungi to antifungal agents.[XXVI] The disk diffusion method for yeasts was developed using the approved standard method (M44-P).[XXVII] Plates inoculated with filamentous fungi, such as *Aspergillus flavus*, were incubated at 25 °C for 48 h; they were incubated at 35-37 °C for 24-48 h, and yeast as *Candida albicans* incubated at 30 °C for 24-48 h, and then the diameters of the inhibition zone were measured in millimeters.[XXVI] The standard disk of amphotericin B (antifungal agent) served as a positive control for antimicrobial activity, but filter disks impregnated with 10 μ L of solvent (distilled water, chloroform, and DMSO) were used as a negative control. The agar used is Mueller-Hinton agar, which is rigorously tested for composition and pH. Further, the depth of the agar in the plate is a factor to be considered in the disk diffusion method. This method is well documented, and standard zones of inhibition have been determined for susceptible and resistant values. Blank paper disks (Schleicher and Schuel, Spain) with a diameter of 8 mm were impregnated with 10 μ L of the test concentration of the stock solutions. When a filter paper disk impregnated with a tested chemical is placed on agar, the chemical will diffuse from the disk into the agar. This diffusion will place the chemical in the agar only around the disk. The solubility of the chemical and its molecular size will determine the size of the area of chemical infiltration around the disk. If an organism is placed on the agar, it will not grow in the area around the disk if it is susceptible to the chemical. This area of no growth around the disk is known as a “zone of inhibition” or “Clear zone. For the disk diffusion, the zone diameters were measured with slipping calipers of the National Committee for Clinical Laboratory Standards [XXVIII]. Agar-based methods, such as the E test and disk diffusion, can be good alternatives because they are simpler and faster than broth-based methods [XXIX, XXX].

Conclusion

This study successfully demonstrates the use of Kinnow peel powder as a green and renewable catalyst for the synthesis of indene-1,3(2H)-dione derivatives (**3a-f**) *via* the Schiff base reaction

between ninhydrin and various aromatic amines. The reaction proceeds under mild conditions (room temperature with stirring), yielding products in good to excellent yields (75% to 92%). Kinnow peel powder as a catalyst facilitates the reaction and eliminates the need for toxic reagents and harsh reaction conditions, aligning with the principles of green chemistry. The eco-friendly nature of this process is further highlighted by using agricultural waste (Kinnow peel) as a catalyst, which promotes sustainability and reduces environmental impact. The synthesized compounds were characterized using elemental analysis, UV, and IR spectroscopy, confirming the formation of the desired products. Additionally, the antifungal evaluation of the synthesized compounds (**3a-f**) revealed promising antifungal activity, suggesting their potential as effective antibacterial agents. By integrating green chemistry principles with synthetic efficiency, this study contributes to the development of sustainable methodologies for the synthesis of biologically active compounds, paving the way for further exploration of Kinnow peel powder in other organic transformations and pharmaceutical applications.

Conflict of interest

The authors declare there is no conflict of interest.

Acknowledgments

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