EFFICIENT BIOLOGICAL ACTIVITY OF ACRIDINE SYNTHESISED BY MICROWAVE IRRADIATION WITH AN EFFICIENT NANOCATALYST

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ABSTRACT
A novel 9-(4-methoxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (MPTH) were synthesized by microwave method by using efficient nano TiO₂ catalyst; nanocatalyst was characterized by XRD and SEM. The compound was analyzed by NMR, mass spectral and biological activity like anticancer was carried out. MPTH was analyzed anticancer action by human blood cell (HRBC) covering stabilization method.

Keywords: MPTH, Microwave, NMR, XRD, SEM, Anticancer.

INTRODUCTION
Multicomponent reactions reactants react in a solo event, but successively, to appearance a novel product, which contains the important parts of beginning resources. MCRs get together the necessities of an environmentally responsive progression, with fewer synthetic steps and fewer energy use and waste production. The varied, reusable catalyst makes these reactions dominant immature chemical knowledge measures, consequential in the least toxic waste and waste material. The growth of new, water charitable acid catalysts can have the most important industrial applications. Acridine-1,8-diones containing significant thought by their possible pharmacological activity against malaria, cancer and leishmania, attach to and photo-damage DNA, are cytotoxic and building block potassium channels.

Acridinediones are synthesized in aqueous media; but, lots of the methods described contain drawbacks, such as the employ of dangerous natural solvents, extensive reaction times, little yields, development of elevation yield and multistep synthesis. During our studies the 9-(4-methoxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione was efficiently catalyzed by synthesis of 9-(4-methoxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione by using microwave at 70 °C. The rutile TiO₂ was synthesized by the sol–gel method and analyzed XRD, HR-SEM. TiO₂–SO₄ has been prepared by the sol–gel method using H₂SO₄ and used for the synthesis of chalcones under microwave irradiation. This catalyst gives an excellent yield with less reaction time and is an inexpensive, easily recyclable catalyst for this reaction.

EXPERIMENTAL
Materials and Measurements
Dimedone, methoxybenzaldehyde and ammonium acetate were purchased by Sigma-Aldrich (St.Louis, USA). ¹H NMR (400 MHz) and ¹³C NMR (400 MHz) spectra were recorded on Brucker spectrometer using DMSO. Microwave irradiation did by Godrej GMS 17M 07 WHGX. XRD was recorded and samples using X–ray Rigaku diffractometer with Cu Kα source (30 kV , 100 mA), at a scan speed of 3.0000 deg/min, step width of 0.1000 deg, in a 2θ range of 20-80°. SEM is recorded JEOL JSM-5610 prepared with back electron detector.
Synthesis of 9-(4-methoxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione

5,5-dimethylcyclohexane-1,3-dione (0.002 mmol) react with ammonium acetate (0.001 mmol) and methoxybenzaldehyde (0.1 mmol) in microwave irradiation with a pinch of efficient nanocatalyst at a suitable time (Table 1). The growth of the result was monitored on TLC (Scheme 1). Following the conclusion of the result was quenched in ice water and filtered, then dried.

![Scheme-1](image1.png)

**Table-1: Melting Point, Yield and Time took for Microwave Method**

<table>
<thead>
<tr>
<th>Compound</th>
<th>MP (°C)</th>
<th>Yield (%)</th>
<th>Microwave Time (min)</th>
<th>Catalyst</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPTH</td>
<td>302-305</td>
<td>75</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>MPTH</td>
<td>303</td>
<td>94</td>
<td>3</td>
<td>TiO₂</td>
</tr>
</tbody>
</table>

9-(4-methoxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione

Anal. calcd. for C_{24}H_{29}NO_{3}: C, 75.96; H, 7.70; N, 3.69. Found: C, 75.94; H, 7.69; N, 3.68. ¹H & ¹³C NMR (400 MHz, DMSO): δ 0.86 (s, 6H), 1.00 (s, 6H), 1.97 (d, J= 10.0 Hz, 2H), 2.16 (d, J= 12.2 Hz, 2H), 2.28-2.52 (m, 2H), 2.51 (d, J= 10.2 Hz, 2H), 3.88 (s, 3H), 4.74 (s, 1H), 6.69 (d, J= 8.8 Hz, 2H), 7.03 (d, J= 8.9 Hz, 2H), 9.27 (s, 1H) (Figure 1a); 5.20, 26.92, 29.57, 32.30, 32.59, 50.72, 63.17, 112.17, 113.84, 128.96, 139.82, 149.57, 156.84, 194.96 (Figure 1b). MS: m/z. 379.49 [M+].

Sol-gel Synthesised TiO₂

The TiO₂ nanocrystal was arranged by sol-gel hydrolysis of (C_{12}H_{28}O_{4}Ti), followed by calcination. About 1ml of titanium isopropoxide (C_{12}H_{28}O_{4}Ti) was soluble in 20 ml isopropyl alcohol and the result was dropped into 10 ml of distilled water, pH 2-6 was in tune by 1M HNO₃ for acidic condition and 1M NaOH for basic condition, exciting a combination of water to alkoxide was added. The former colorless sol-gel of hydrous oxide was stimulated strongly for 2 hrs at space heat and then permissible to overnight. The resultant substance was dried and calcinated at 500 °C for 2 hrs.

MTT Assay

The cytotoxic progress of the compound was resolved to utilize MTT measure. 1x10⁴ cells for every cell were seed in 100 mL DMEM (Dulbecco’s Modified Eagle Medium), it was added with 10% FBS (Fetal Bovine Serum) in every well of 96-well microculture plates and brooded at 37°C for 24 h in a CO₂ hatchery. Subsequent to 48 h of hatching, 10 mL MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl
tetrazoliumbromide (5 mgmL⁻¹) has supplemented to every cell and the dishware was additionally brooded for 4 h. At that point, the supernatant from every well was painstakingly evacuated, formazan gems were broken down in 100 mL DMSO and the absorbance was recorded at 570 nm wavelength.

RESULTS AND DISCUSSION

XRD and SEM

XRD of TiO₂ nanoparticle obtain by sol-gel technique (Fig.-2), the XRD of TiO₂ match with JCPDS pattern of (89-4921), body-centered tetragonal with crystal constants a = b =3.7774Å and c = 9.501 Å. The crystallite sizes (L) of TiO₂ as 10.44 nm, Full width at half maximum of the most strong peaks of the individual crystals using the Scherrer equation, L = 0.9 λ / βcosθ, where λ is the wavelength of the X-rays used, θ is diffraction angle and β is the full width at half maximum of the peak. The particular surface area of the nanocrystal has been deduced by employing the association S = 6/ρD, where S is the specific outside area and ρ is the substance density. The designed surface area for TiO2 is 140.32 m²/g. The SEM of TiO₂ nanocrystal was displayed in Fig.-3. The calculated crystallite sizes agree with that obtained by XRD.
Cytotoxicity

The manufactured compound was subjected to the *in vitro* anticancer consequence of spirooxindole in KB cancer cell line. Spirooxindole action 24-h incubation considerably reduced the percentage of cell feasibility in KB cancer cells. This recommended that spirooxindole management has tendency to restrain the enlargement of cancer cells through incubation. The reaction of cytotoxicity of compound MPTH with their applications is given in Figs.-4a and 4b.
These outcomes executed MTT test in KB cancer cells which is treated with similar concentrations of compounds for up to 24h. The results of the compound MPTH display wide inhibitions on the KB cell appearance with IC\textsubscript{50} values of 25.06 µg. The IC\textsubscript{50} values of the MPTH imply that methoxy substituted compounds hold more inhibitory effects against the cancer cells.

**CONCLUSION**

An efficient MPTH moiety was synthesized by microwave method by using efficient nanocatalyst with effortlessness, high yield, eco-friendly conditions. The crystallite sizes (L) and surface area (S) of TiO\textsubscript{2} as 10.44 nm, 140.32 m\textsuperscript{2}/g. MPTH displays wide inhibitions on the KB cell appearance with IC\textsubscript{50} values 25.06 µg. The IC\textsubscript{50} values of the MPTH imply that methoxy substituted compounds hold more inhibitory effects against the cancer cells.

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