Research Article

Sonochemical Synthesis of Some Novel Triazoloquinazolinones using Silica Iodide as a Heterogeneous Catalyst and their Biological Evaluation

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Abstract: Functionalized silica based reagent: SiO_2 -I has been found to be an efficient heterogeneous catalyst for the reaction of aromatic aldehydes, 3-amino-1,2,4-triazole and dimedone to afford novel triazoloquinazolinones under sonication. The method is green as it involves use of a heterogeneous catalyst and an energy efficient technique. The products are formed in very high yields; and the catalyst can be recycled for at least four times without significant loss of the catalytic activity. All the obtained compounds were analyzed for *in-vitro* antiproliferative activity against human cancer cell line (HeLa) by MTT assay. The results showed that, all the compounds possess antiproliferative activity; and compound **4a** exhibited the least IC₅₀ value of 20.2 μ g/mL.

Keywords: Triazoloquinazolinones, 3-amino-1,2,4-triazole, silica iodide, sonication, HeLa cell lines, MTT assay.

1. INTRODUCTION

Green chemistry concepts motivate the chemical and pharmaceutical industries to consider the crash on human life when the new heterocyclic compounds are introduced into our society. The principle behind this concept is to develop eco-friendly and environment friendly approaches for the preparation of biologically active compounds by employing energy efficient greener protocols [1].

Heterocyclic compounds; in particular, the nitrogen heterocycles, play an important role in the biological and medicinal chemistry. Nitrogen-containing compounds are widely distributed in nature and have played a vital role and have gained importance in the agrochemical and pharmaceutical industries [2]. The ring-fused heterocyclic system: quinazolinone, constitutes an important class of heterocyclic motif, which is found as a core structural skeleton in a variety of natural products; and in more than 100 naturally occurring alkaloids [3]. The quinazolinone framework and its derivatives (**Figure 1**) have been broadly studied because of their wide range of pharmacological activities such as antifungal,

antimicrobial, antitubercular, anticancer, anti-HIV, antiulcer, anti-inflammatory, antidepressant, immunotropic, analgesic and anticonvulsant activities [4].



Figure 1. Some selected examples of biologically active quinazolinones

Search for anticancer agents is a challenging call in the field of medicinal chemistry. Even though chemotherapy is being used as a standard treatment method for cancer [5], cancer has always been a major threat to the human life. Thus, search for a newer class of the anticancer agents has increased in recent years, and there has been a rigorous search for the discovery and development of novel selective anticancer agents, which are devoid of many of the unpleasant side effects of conventional anticancer agents [6].

Ultrasound is an imperative tool in sonochemistry and has proved to be advantageous with the use of smaller quantities of hazardous chemicals and solvents; increase in the product selectivity under low energy consumption. Thus, for various synthetic routes, sonochemistry finds the receptive approach in the green chemistry. Under sonication the system is facilitated with the physical and chemical effects together with the effect of shock waves acting on the collapse of bubbles that pronounces it to be the convenient and practical tactic in organic synthesis. In employing the greener methodology, ultrasound, provides a well understanding that, it benefits in improvising the reaction rates and the product yields [7].

A few synthetic strategies have been documented in the literature for the synthesis of quinazolinones [8], and some of these methods are associated with one or more disadvantages such as: extensive reaction time, harsh reaction conditions, inadequate yields, tedious work-up procedures, use of environmentally toxic reagents or solvents and use of large amounts of solid supports which results in the generation of a huge amount of toxic waste.

Silica based catalysts have been used to catalyze some important organic transformations [9], and are explored to be potent catalysts owing to the various advantages offered by them including the environment friendly component such as: broad transformation skills, stability and non-corrosive nature, excellent catalytic activity, low levels of toxicity, operational simplicity, *Borderless Science Publishing* 181

commercial availability and low cost. In the present report, the use of a heterogeneous system with the application of ultrasound has singly provided the methodical make over and has effectively proved to be the simple, efficient, mild and better yielding green synthetic protocol for the synthesis of some novel quinazolinone derivatives.

In view of the biological importance of these N-heterocyclic compounds, it was planned to synthesize a series of novel quinazolinone derivatives by a one-pot three-component reaction under ultrasonic irradiation as shown in the **Scheme 1**. The synthesized quinazolinone derivatives have been evaluated for *in vitro* antiproliferative activity against cervical carcinoma cell line HeLa using MTT assay.



Scheme 1. Synthesis of 9-(aryl)-6,6-dimethyl-5,6,7,9-tetrahydro-4*H*-[1,2,4]-triazolo-[5,1*b*]-quinazolin-8(4*H*)-ones in the presence of silica iodide.

2. EXPERIMENTAL

2.1 Materials and Methods

All starting reagents and solvents were commercial products and were used without further purification except liquid aldehydes which were distilled before use. Yields refer to yield of the isolated products. Melting points were determined in capillary tubes using a Raaga, INDIAN make melting point apparatus. Nuclear magnetic resonance spectra were obtained on a Bruker AMX instruments in CDCl₃ using TMS as an internal standard [400 MHz and 100 MHz for ¹H NMR for ¹³C NMR respectively]. ESI-Mass spectra were recorded on ESI-Q TOF instrument. Infrared spectra were recorded using Cary FT-IR 630s spectrophotometer. CHN analysis was performed using Elementar vario MICRO cube analyzer. All the reactions were studied using SIDILU, INDIAN make sonic bath working at 35 kHz (constant frequency) maintained at 25 °C by circulating water continuously without mechanical stirring.

2.2 Typical procedure for the synthesis of Triazoloquinazolinones under ultrasonication

A mixture of aromatic aldehyde (1 mmol), dimedone (1 mmol), 3-amino-1,2,4-triazole (1 mmol) and silica iodide (0.1 g) were taken in acetonitrile (5 mL) and sonicated in a sonic bath working at 35 kHz

(constant frequency, maintained at 25 °C by circulating water) for 30–40 min. The completion of the reaction was monitored by TLC, and the resulting solid material was dissolved in hot ethanol, filtered to remove the catalyst and then the filtrate was cooled to afford the pure product. The solid catalyst thus separated was kept aside for further use.

2.3 Spectral Data

9-(3-Hydroxy-4-methoxy-phenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-4H-[1,2,4]triazolo[5,1-b]quinazolin-8-one (4a)

Colorless solid, Mp 213–215 °C; **IR** (**ATR**): v 3350 (OH), 2850–2950 (NH), 1600 (C=O) cm⁻¹; ¹**H NMR** (CDCl₃, 400 MHz): δ 1.25 (s, 3H, CH₃), 1.31 (s, 3H, CH₃), 2.21–2.31 (m, 4H, 2CH₂), 3.75 (s, 3H, OCH₃), 5.10 (s, 1H, OH), 5.70 (s, 1H, CH), 6.73 (s,1H, Ar-H), 6.90–6.91 (d, 1H, *J* = 4.4Hz, Ar-H), 7.05–7.06 (d, 1H, *J* = 4.4Hz, Ar-H), 8.73 (s, 1H, =CH), 10.75 (s, 1H, NH) ppm. ¹³**C NMR** (CDCl₃, 100MHz): δ 16.08, 27.65, 41.14, 50.90, 54.20, 59.76, 102.61, 109.08, 127.29, 130.10, 132.16, 138.11, 139.32, 145.10, 167.55, 195.64 ppm. **ESI-MS**: [M⁺] 340.10. **Anal. Calcd for** C₁₈H₂₀N₄O₃ : C, 63.52; H, 5.92; N, 16.46; **Found**: C, 63.52; H, 5.90; N, 16.46.

9-(3-Bromo-4-methoxy-phenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-4H-[1,2,4]triazolo[5,1 b]quinazolin-8-one (4b)

Colorless solid, Mp 204–205 °C; **IR** (**ATR**): υ 3225 (OH), 2850–2950 (NH), 1600 (C=O)cm⁻¹; ¹**H NMR** (CDCl₃, 400 MHz): δ 1.12 (s, 3H, CH₃), 1.27 (s, 3H, CH₃), 2.31–2.52 (m, 4H, 2CH₂), 3.73 (s, 3H, OCH₃), 5.54 (s, 1H, CH), 7.39–7.41 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.42 (s,1H, Ar-H), 7.44–7.46 (d, 1H, *J* = 8.0 Hz, Ar-H), 8.00 (s, 1H, =CH), 11.86 (s, 1H, NH) ppm. ¹³C **NMR** (CDCl₃, 100 MHz): δ 24.91, 29.78, 31.48, 31.96, 40.38, 41.63, 121.13, 122.31, 123.79, 124.42, 127.75, 129.34, 135.05, 147.23, 154.63, 163.19, 189.11 ppm. **ESI-MS**: [M⁺] 402.10. **Anal.Calcd for** C₁₈H₁₉BrN₄O₂: C, 53.61; H, 4.75; N, 13.89; **Found**: C, 53.61; H, 4.78; N, 13.86.

6,6-Dimethyl-9-(3,4,5-trimethoxy-phenyl)-5,6,7,9-tetrahydro-4H-[1,2,4]triazolo[5,1b]quinazolin-8-one (4c)

Colorless solid, Mp 243–245 °C; **IR** (**ATR**): υ 3330 (NH), 1620 (C=O) cm⁻¹; ¹**H NMR** (CDCl₃, 400 MHz): δ 0.96 (s, 3H, CH₃). 1.04 (s, 3H, CH₃), 2.12–2.30 (m, 4H, 2CH₂), 3.73 (s, 3H, OCH₃), 3.76 (s, 6H, 2OCH₃), 5.02 (s, 1H, CH), 6.95 (s, 2H, Ar-H), 8.12 (s, 1H, =CH), 10.17 (s, 1H, NH) ppm. ¹³CNMR (CDCl₃, 100 MHz): δ 16.39, 26.28, 26.78, 42.21, 46.39, 55.02, 60.03, 106.15, 110.00, 117.74, 131.43, 132.05, 132.82, 135.30, 150.80, 164.03, 190.80 ppm. **ESI-MS**: [M⁺] 384.10. **Anal.Calcd for** C₂₀H₂₄N₄O₄: C, 62.49; H, 6.29; N, 14.57; **Found**: C, 62.31; H, 6. 28; N, 14.41.

9-(5-Bromo-2-hydroxy-phenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-4H-[1,2,4]triazolo[5,1-b]quinazolin-8-one (4d)

Colorless solid, Mp 209–210 °C; IR (ATR): v 3300 (OH), 2925–3010 (NH), 1600 (C=O) cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 1.05 (s, 3H, CH₃), 1.20 (s, 3H, CH₃), 2.27–2.50 (m, 4H, 2CH₂), 3.70 (s, 1H, OH), 5.84 (s, 1H, CH), 6.232–6.236 (d, 1H, J = 1.6 Hz, Ar-H), 6.25 (s, 1H, Ar-H), 6.87–6.88 (d, 1H, J = 1.6 Hz, Ar-H), 8.39 (s, 1H, =CH), 11.10 (s, 1H, NH) ppm. ¹³CNMR (CDCl₃, 100 MHz): δ 16.97, 26.92, 32.90, 47.21, 50.49, 55.99, 104.28, 104.70, 115.69, 125.61, 133.87, 136.04, 152.96, 153.48, 189.42, 190.52 ppm. **ESI-MS**: [M+1] 389.70. **Anal.Calcd for** C₁₇H₁₇BrN₄O₂: C, 52.46; H, 4.40; N, 14.39; **Found**: C, 52.41; H, 4.38; N, 14.39.

9-(3,5-Dibromo-2-hydroxy-phenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-4H-[1,2,4]triazolo[5,1-b]quinazolin-8-one (4e)

Colorless solid, Mp 238–240 °C; **IR** (**ATR**): υ 3000–3100 (NH), 1650 (C=O) cm⁻¹; ¹**H NMR** (CDCl₃, 400 MHz): δ 0.87 (s, 3H, CH₃), 1.01 (s, 3H, CH₃), 1.98–2.37 (m, 4H, 2CH₂), 3.90 (s, 1H, OH), 5.80 (s, 1H, CH), 7.52 (s, 1H, Ar-H), 7.60 (s, 1H, Ar-H), 8.40 (s, 1H, =CH), 12.02 (s, 1H, NH) ppm. ¹³**C NMR** (CDCl₃, 100 MHz): δ 16.85, 26.77, 32.44, 41.30, 43.35, 50.05, 50.70, 111.01, 111.19, 116.85, 117.79, 128.02, 129.93, 133.78, 168.52, 180.70 ppm. **ESI-MS**: [M⁺] 465.90. **Anal.Calcd for** C₁₇H₁₆Br2N₄O₂: C, 43.62; H, 3.44; N, 11.97. **Found**: C, 43.61; H, 3.40; N, 11.97.

9-(2-Fluoro-phenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-4H-[1,2,4]triazolo[5,1-b]quinazolin-8-one (4f)

Colorless solid, Mp 228–230 °C; **IR** (**ATR**): v 2900–3100 (NH), 1601(C=O) cm⁻¹; ¹**H NMR** (CDCl₃, 400 MHz): δ 1.25 (s, 3H, CH₃) 1.35 (s, 3H, CH₃), 2.42–2.49 (m, 4H, 2CH₂), 5.44 (s, 1H, CH), 6.90–6.92 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.21–7.28 (m, 2H, Ar-H), 7.76–7.78 (d, 1H, *J* = 8.0 Hz, Ar-H), 8.07 (s, 1H, NH), 10.05 (s, 1H, NH) ppm. ¹³**C NMR** (CDCl₃, 100 MHz): δ 19.42, 27.03, 36.54, 49.44, 55.84, 100.10, 105.50, 106.28, 111.12, 124.35, 125.70, 132.46, 149.44, 152.11, 168.10, 195.72 ppm. **ESI-MS**: [M+2] 314.10. **Anal.Calcd for** C₁₇H₁₇FN₄O: C, 65.37; H, 5.49; N, 17.94; **Found**: C, 65.31; H, 5.48; N, 17.92.

9-(4-Chloro-3-fluoro-phenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-4H-[1,2,4]triazolo[5,1-b] quinazolin-8-one (4i)

Colorless solid, Mp 259–260 °C; **IR** (**ATR**): v 3325–3400 (NH), 1680–1700 (C=O) cm⁻¹; ¹**H NMR** (CDCl₃, 400 MHz): δ 0.91 (s, 3H, CH₃), 1.08 (s, 3H, CH₃), 1.98–2.37 (m, 4H, 2CH₂), 5.80 (s, 1H, CH), 7.32–7.34 (d, 1H, *J* = 7.6 Hz, Ar-H), 7.38 (s, 1H, Ar-H), 7.40–7.42 (d, 1H, *J* = 8.0 Hz, Ar-H), 8.35 (s, 1H, =CH), 11.65 (s, 1H, NH) ppm. ¹³C **NMR** (CDCl₃, 100 MHz): δ 20.09, 24.55, 34.34, 60.29, 65.99, 117.24, 117.90, 118.28, 121.09, 122.23 131.12, 142.21, 145.80, 149.68, 152.45, 161.16, 200.09 ppm. **ESI-MS**: [M⁺] 346.10. **Anal. Calcd for** C₁₇H₁₆ClFN₄O: C, 58.88; H, 4.65; N, 16.16; **Found**: C, 58.81; H, 4.65; N, 16.16.

3. RESULTS AND DISCUSSION

3.1 Chemistry

3.1.1 Effect of catalyst

A variety of catalysts were screened in order to validate the right choice and the results of this study are presented in the **Table 1**. To justify the influence of the catalyst, the three-component reaction was first carried out in the presence of catalytic FeCl₃ wherein a maximum yield of only 55% could be obtained (**Table 1**, Entry 1). It was further observed that, the yield of the product hardly improved in the presence of other catalysts (**Table 1**, Entries 2–8), whereas the use of silica iodide as catalyst significantly improved the yield to 90% (**Table 1**, Entry 9). Hence, silica iodide under ultrasonic irradiation was selected for our further studies.

		Reaction Condition					
Enter	Catalant	25 °C		Ret	flux	US	
Enuy	Catalyst	Time	Yield	Time	Yield	Time	Yield
		(min)	$(\%)^{d}$	(min)	$(\%)^{d}$	(min)	$(\%)^{e}$
1	FeCl ₃ ^b	600	14	600	35	30	55
2	DABCO ^b	600	15	600	30	30	60
3	Glycine ^b	600	10	600	35	30	65
4	Na ₂ CO ₃ ^b	600	10	600	30	30	60
5	$K_2 CO_3^{b}$	600	13	600	25	30	55
6	$Cs_2CO_3^{b}$	600	15	600	30	30	65
7	InCl ₃ ^b	600	14	600	20	30	65
8	Amberlite ^c	600	10	600	30	30	60
9	SiO ₂ -I ^c	600	20	600	40	30	90

^a Reaction conditions: Aromatic aldehyde (1 mmol), dimedone (1 mmol), 3-amino-1,2,4-triazole (1 mmol) in CH₃CN (5 mL); ^b10 mol%; ^c 0.1 g; ^dGLC; ^e Isolated yield.

3.1.2 Effect of solvent

We started the work by examining the reaction of 3-hydroxy-4-methoxybenzaldehyde, dimedone and 3-amino-1,2,4-triazole to get 9-(3-hydroxy-4-methoxyphenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-4*H*-[1,2,4]triazolo[5,1-*b*]quinazolin-8-one (**4a**) in different solvents and it was found that, acetonitrile in the presence of catalytic SiO₂-I as a catalyst under sonication afforded 90% of the corresponding product after 30 minutes as shown in the **Table 2** (Entry 10).

3.1.3 Optimization of feed ratio of silica iodide under sonication

Further studies were carried out to optimize the amount of catalyst by using different amounts of SiO_2 -I (0.01, 0.05, 0.10, 0.15, 0.20 and 0.25 g) and the results of this study are presented in the **Table 3**. From this Table, it is clear that, 0.1g of SiO_2-I afforded **4a** in 90% yield (**Table 3**, Entry 4). Increasing the amount of catalyst did not improve the yield of the product.

3.1.4 Synthesis of 4 (a-k) under sonic condition

In order to generalize the method, different substituted aldehydes were treated with dimedone and 3-amino-1,2,4-triazole and the result of this study is presented in the **Table 4**. From the data presented in this Table, it is clear that, the method is effective for both electron withdrawing and electron donating aromatic aldehydes. Later the reactions were carried out using aliphatic aldehydes also (**Table 4**, Entries 10 and 11), and it was found that, there was no product formation even after 15 h.

3.1.5 Effect of sonication

In pronouncing the application of sonication to the present reaction it is necessary to understand the concept of formation and collapse of bubbles in liquid phase and the mechanical effects on solid (heterogeneous) surface. Under the low frequency range 20–40 kHz, the bond dissociation occurs at the cause of both physical and chemical effects, which is very important for the initiation of a chemical reaction, in a heterogeneous medium. In the present reaction, under the influence of ultrasound, the reaction begins in the presence of dispersed particles of SiO₂-I and the partially dissolved reactants in a solvent. A sufficiently large negative pressure applied to the liquid on rarefaction, offers the breakdown of liquid and creates cavitation bubbles. At the solid-liquid interlayer, the asymmetric collapse of the cavitational bubble causes jet impact of the polar solvent (liquid) which is targeted at the surface of the catalyst. The additional nucleation sites for cavitation events over the surface of the catalyst enhance the number of microbubbles in the solution medium. Thus, the formation of jets can improve the mass transfer to the surface of the heterogeneous catalyst. Therefore, the mechanical effects on the solid particles and physical effects in the solution phase generate the collapsing bubble which affects the chemical species in solution and contributes in acceleration of the reaction rates [11].

	Solvent	Reaction condition						
Enter		<u>25 °C</u>		Reflux		<u>US</u>		
Епиу		Time	Yield	Time	Yield	Time	Yield	
		(min)	$(\%)^{b}$	(min)	$(\%)^{b}$	(min)	$(\%)^{c}$	
1	No Solvent	600	-	600	-	30	-	
2	H_2O	600	18	600	30	30	48	
3	Ethanol	600	10	600	20	30	60	
4	1,4-Dioxane	600	12	600	35	30	55	
5	DMF	600	16	600	25	30	40	
6	DMSO	600	15	600	25	30	45	
7	<i>n</i> -Hexane	600	12	600	25	30	59	
8	THF	600	10	600	20	30	60	
9	EtOH-H ₂ O	600	47	600	55	30	70	
10	CH ₃ CN	600	20	600	40	30	90	

Table 2. Optimization of solvent for the synthesis of 4a^a

^a Reaction conditions: Aromatic aldehyde (1 mmol), dimedone (1 mmol), 3-amino-1,2,4-triazole (1mmol), silica iodide (0.1 g) in Solvent (5 mL); ^b GLC; ^c Isolated yield.

Entry	SiO_2 -I (g)	Time (min)	Yield (%) ^a
1	0	480	40
2	0.01	900	50
3	0.05	600	55
4	0.10	30	90
5	0.15	30	90
6	0.20	30	90
7	0.25	30	90

^a Isolated yield

Table 4. Synthesis of triazoquinazolinones 4 (a-k) using SiO₂-I in CH₃CN under sonic condition

					Mp (°C)	
Entry	Aldehydes	Product	Time (min)	Yield (%) ^a	Found	Reported
1	3-HO,4-MeOC ₆ H ₃ CHO	4 a	30	90	213-215 [†]	_
2	3-Br,4-MeOC ₆ H ₃ CHO	4 b	35	87	$204 - 205^{\dagger}$	_
3	3,4,5-MeOC ₆ H ₂ CHO	4 c	30	90	$243 - 245^{\dagger}$	_
4	5-Br,2-HOC ₆ H ₃ CHO	4d	34	86	$209 - 210^{\dagger}$	_
5	2-HO,3,5-BrC ₆ H ₂ CHO	4e	30	85	$238 - 240^{\dagger}$	_
6	2-FC ₆ H ₄ CHO	4f	40	82	$228 - 230^{\dagger}$	_
7	2,4-ClC ₆ H ₃ CHO	4 g	30	80	323-324	323-325 [10]
8	2,4-MeOC ₆ H ₃ CHO	4h	38	89	210-212	210-212 [10]
9	3-F,4-ClC ₆ H ₃ CHO	4 i	30	87	$259 - 260^{\dagger}$	_
10	НСНО	4 j	15.0	ND	_	_
11	CH ₃ CHO	4 k	15.0	ND	—	_

^a Isolated yield; [†]Novel compound; ND: not detected

3.2 Biology

3.2.1 Methodology

3.2.1.1 Cell culture

HeLa cell line was maintained in DMEM medium (GIBCO) supplemented with 10% (v/v) heat-inactivated fetal bovine serum (FBS) and 1% antibiotic solution (penicillin 100 Uml^{-1} and streptomycin 100 μgml^{-1}) at 37 °C in a humidified atmosphere of 95% air with 5% CO₂. The medium was changed every second day, and cells were sub-cultured when confluency reached to

95% by 0.25% trypsin containing 0.02% ethylenediaminetetraacetic acid (EDTA) in PBS for 3 min at 37 $^{\circ}$ C.

3.2.1.2 MTT Assay

The MTT assay was carried out as described previously to measure cell viability [12]. Ten thousand cells in 100 μ L of DMEM media were seeded in the wells of a 96-well plate. After 24 h, the existing medium was removed and 100 μ L of various concentrations of the synthesized compounds were added and incubated for 48 h at 37 °C in a CO₂ incubator.

Control cells were supplemented with 0.05% DMSO vehicle. At the 48th hour of incubation, MTT 3-(4,5-dimethylthaizol-2-yl)-2,5-diphenyltetrazolium bromide supplied from Sigma (10 μ L of 5 mg/mL) was added to the plate. The contents of the plate were pipetted out carefully, the formazan crystals formed were dissolved in 100 μ L of DMSO, and the absorbance was measured at 550 nm in a microplate reader (Tecan, infinite F200 Pro). Experiments were performed in triplicate, and the results were expressed as mean of percent inhibition. A graph of the concentration versus percent growth inhibition was plotted, and the concentration at which 50% cell death occurred was considered as the IC₅₀ value. Before adding MTT, images (Olympus 1X81, cell Sens Dimension software) were taken for visualizing the cell death.

3.2.1.3 Results

The IC₅₀ values obtained for the prepared products (4a-h) demonstrated that, all of them are cytotoxic in nature, and showed inhibitory activity against HeLa cell lines. Out of the eight compounds, **4a** showed relatively good activity with respect to the standard drug doxorubicin. The results of these studies are presented in the **Table 5** and as a bar diagram in the **Figure 2**. Microscopic images of the HeLa cancer cell death caused by the compound **4a** is presented in the **Figure 3**.

Tested compounds	IC_{50} values (µg/mL)		
$4a^{\dagger}$	20.2±0.59		
4b	40.5 ± 0.70		
$4c^{\dagger}$	24.3±0.17		
4d	32.5±0.14		
4e	33.2±0.78		
4f	28.6±0.95		
4g	35.9±0.31		
4h	30.2±0.17		
Doxorubicin	10.6±0.12		
[†] Active compounds; Data given is Mean \pm SE (n = 3)			

Table 5. IC₅₀ values of tested compounds 4 (a-h) and the standard drug doxorubicin



Figure 2. IC₅₀ values of tested compounds 4 (a-h) and standard drug doxorubicin.



Figure 3. Antiproliferative activity of compound 4a (A-control; B-treated)

4. CONCLUSION

In conclusion, we have developed a facile and an energy efficient method for the synthesis of a series of known and novel triazoloquinazolinone derivatives in the presence of catalytic silica iodide in acetonitrile medium. The salient features of this green protocol are: formation of single product under sonication, acceleration of the rate of the reaction, the method involves simple work-up procedure, high to excellent yields of the products and shorter reaction durations and reusability of silica iodide catalyst. Advancement to the present study includes the *in vitro* studies on the synthesized compounds, which indicated that, **4a** and **4c** exhibited better anti-proliferative activity when compared to the other

derivatives. Further work on the synthesis and biological studies of such similar derivatives will be taken up in due course of time in order to develop much better compounds for the treatment of different types of cancer.

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The authors declare no conflict of interest

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